

FOR OFFICIAL USE ONLY

ACCESS DB # 190367
PLEASE PRINT CLEARLY

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Roy P. Issac Examiner #: 82353 Date: 4/5/18/06
Art Unit: 1623 Phone Number: 2-2674 Serial Number: 10/654365
Location (Bldg/Room#): 5D24 (Mailbox #): 5D24 Results Format Preferred (circle): PAPER DISK or Email

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

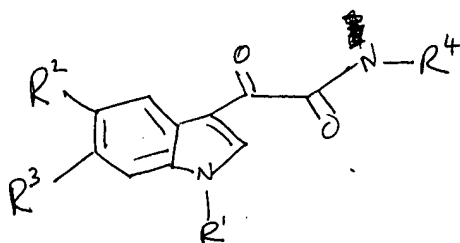
Title of Invention: TREATMENT OF NON-ALLERGIC RHINITIS BY SELECTIVE
PHOSPHODIESTERASE-4
Inventors (please provide full names): RUMFELDT, C; ~~THE~~
REBE HILDEGARD, K; HOFGEN, N;

Earliest Priority Date: 06 September 2002

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



\$ 25.61
15 min

STAFF USE ONLY

Searcher: [Signature]

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: 5/19/06

Date Completed: 5/23/06

Searcher Prep & Review Time: 45

Online Time: 60

Type of Search

____ NA Sequence (#)

____ AA Sequence (#)

____ Structure (#)

____ Bibliographic

____ Litigation

____ Fulltext

____ Other

Vendors and cost where applicable

☒ STN _____ Dialog

____ Questel/Orbit _____ Lexis/Nexis

____ Westlaw _____ WWW/Internet

____ In-house sequence systems

____ Commercial _____ Oligomer _____ Score/Length
____ Interference _____ SPDI _____ Encode/Transl

____ Other (specify)

65

=> d his nofile

(FILE 'HOME' ENTERED AT 09:41:00 ON 23 MAY 2006)
D SAVE

FILE 'CAPLUS' ENTERED AT 09:41:35 ON 23 MAY 2006
ACTIVATE KUSS/A

L1 (74)SEA ABB=ON PLU=ON ("RUNDFELDT C"/AU OR "RUNDFELDT CHRIS"/AU)
L2 (51)SEA ABB=ON PLU=ON ("KUSS H"/AU OR "KUSS H H"/AU OR "KUSS H
J"/AU OR "KUSS H M"/AU OR "KUSS HILDEGARD"/AU)
L3 (12)SEA ABB=ON PLU=ON ("HOFGEN N"/AU OR "HOFGEN NORBERT"/AU)
L4 9 SEA ABB=ON PLU=ON (L1 AND (L2 OR L3)) OR (L2 AND L3)

ACTIVATE KUSSALL/A

L5 (74)SEA ABB=ON PLU=ON ("RUNDFELDT C"/AU OR "RUNDFELDT CHRIS"/AU)
L6 (51)SEA ABB=ON PLU=ON ("KUSS H"/AU OR "KUSS H H"/AU OR "KUSS H
J"/AU OR "KUSS H M"/AU OR "KUSS HILDEGARD"/AU)
L7 (12)SEA ABB=ON PLU=ON ("HOFGEN N"/AU OR "HOFGEN NORBERT"/AU)
L8 126 SEA ABB=ON PLU=ON (L5 OR L6 OR L7)

D QUE L8

FILE 'CAPLUS' ENTERED AT 09:47:33 ON 23 MAY 2006

FILE 'REGISTRY' ENTERED AT 09:48:56 ON 23 MAY 2006

L9 STRUCTURE UPLOADED
L10 QUE ABB=ON PLU=ON L9
D L9
L11 0 SEA SSS SAM L9

FILE 'STNGUIDE' ENTERED AT 09:49:33 ON 23 MAY 2006

FILE 'REGISTRY' ENTERED AT 10:59:41 ON 23 MAY 2006

D L9
L12 1 SEA SSS FUL L9
D SCAN

FILE 'CAPLUS' ENTERED AT 11:05:32 ON 23 MAY 2006

E US2003-654365/APPS
L13 1 SEA ABB=ON PLU=ON US2003-654365/AP
SEL RN L13

FILE 'REGISTRY' ENTERED AT 11:05:54 ON 23 MAY 2006

L14 4 SEA ABB=ON PLU=ON (257892-33-4/BI OR 671801-81-3/BI OR
671801-82-4/BI OR 9036-21-9/BI)
D SCAN
D L14 1
L15 STR 671801-82-4

FILE 'STNGUIDE' ENTERED AT 11:15:43 ON 23 MAY 2006

FILE 'REGISTRY' ENTERED AT 11:21:18 ON 23 MAY 2006

L16 STRUCTURE UPLOADED
L17 QUE ABB=ON PLU=ON L16
L18 2 SEA SSS SAM L16

D SCAN

L19 35 SEA SSS FUL L16

FILE 'CAPLUS' ENTERED AT 11:22:00 ON 23 MAY 2006

L20 51 SEA ABB=ON PLU=ON L19
L21 10 SEA ABB=ON PLU=ON L20 NOT (PY>2002 OR AY>2002 OR PRY >2002)
L22 11 SEA ABB=ON PLU=ON L20 AND L8
L23 19 SEA ABB=ON PLU=ON (L22 OR L21)
L24 14 SEA ABB=ON PLU=ON (L4 OR L22)
L25 40 SEA ABB=ON PLU=ON L20 NOT L22

FILE 'REGISTRY' ENTERED AT 11:24:26 ON 23 MAY 2006

L26 ANALYZE PLU=ON L19 1-35 RN : 35 TERMS
D

FILE 'CAPLUS' ENTERED AT 11:25:27 ON 23 MAY 2006

L27 ANALYZE PLU=ON L20 1-51 RN : 2229 TERMS
D

FILE 'REGISTRY' ENTERED AT 11:26:11 ON 23 MAY 2006

L28 1 SEA ABB=ON PLU=ON 257892-33-4
D SCAN

L29 34 SEA ABB=ON PLU=ON L19 NOT L28

FILE 'CAPLUS' ENTERED AT 11:26:38 ON 23 MAY 2006

L30 10 SEA ABB=ON PLU=ON L29

=> file caplus

FILE 'CAPLUS' ENTERED AT 11:28:38 ON 23 MAY 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 23 May 2006 VOL 144 ISS 22

FILE LAST UPDATED: 22 May 2006 (20060522/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

<http://www.cas.org/infopolicy.html>

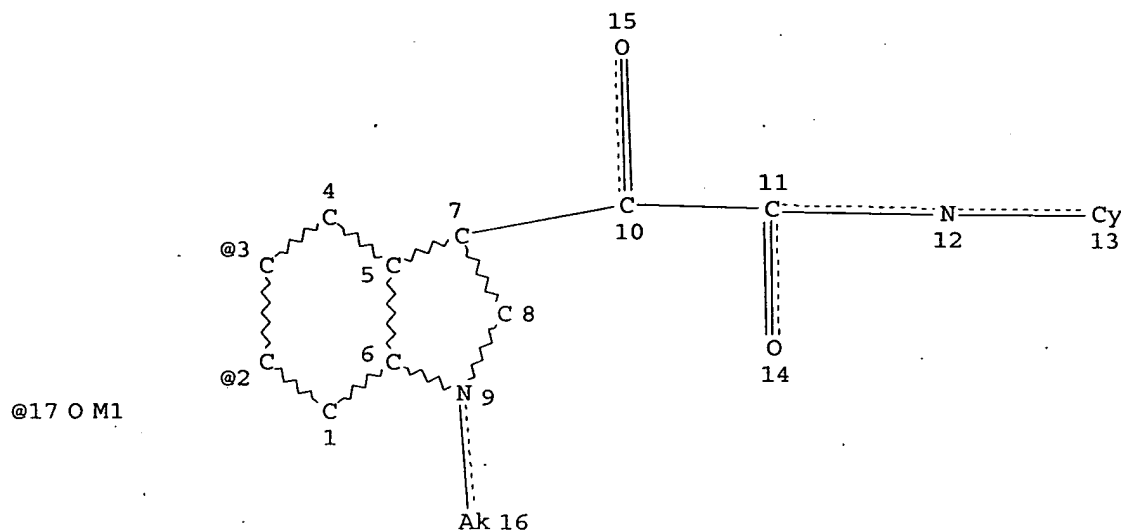
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que l25

L5 (74)SEA FILE=CAPLUS ABB=ON PLU=ON ("RUNDFELDT C"/AU OR "RUNDFELDT CHRIS"/AU)
L6 (51)SEA FILE=CAPLUS ABB=ON PLU=ON ("KUSS H"/AU OR "KUSS H H"/AU OR "KUSS H J"/AU OR "KUSS H M"/AU OR "KUSS HILDEGARD"/AU)
L7 (12)SEA FILE=CAPLUS ABB=ON PLU=ON ("HOFGEN N"/AU OR "HOFGEN

NORBERT"/AU)

L8 126 SEA FILE=CAPLUS ABB=ON PLU=ON (L5 OR L6 OR L7)
 L16 STR



VPA 17-2/3 U

NODE ATTRIBUTES:

HCOUNT	IS M1	AT 17
NSPEC	IS R	AT 1
NSPEC	IS R	AT 2
NSPEC	IS R	AT 3
NSPEC	IS R	AT 4
NSPEC	IS R	AT 5
NSPEC	IS R	AT 6
NSPEC	IS R	AT 7
NSPEC	IS R	AT 8
NSPEC	IS R	AT 9
NSPEC	IS C	AT 10
NSPEC	IS C	AT 11
NSPEC	IS C	AT 12
NSPEC	IS C	AT 13
NSPEC	IS C	AT 14
NSPEC	IS C	AT 15
NSPEC	IS C	AT 16
NSPEC	IS C	AT 17

DEFAULT MLEVEL IS ATOM

MLEVEL IS CLASS AT 10 11 12 14 15 16 17

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE

L19	35 SEA FILE=REGISTRY SSS FUL L16
L20	51 SEA FILE=CAPLUS ABB=ON PLU=ON L19
L22	11 SEA FILE=CAPLUS ABB=ON PLU=ON L20 AND L8
L25	40 SEA FILE=CAPLUS ABB=ON PLU=ON L20 NOT L22

=> d ibib abs hitstr 125 tot

L25 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:365169 CAPLUS

DOCUMENT NUMBER: 144:419682

TITLE: Pharmaceutical compositions containing phosphodiesterase IV inhibitors and immunosuppressants

INVENTOR(S): Harada, Daisuke; Kobayashi, Katsuya; Manabe, Haruhiko; Ohshima, Etsuo

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006041120	A1	20060420	WO 2005-JP18854	20051013
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.:

JP 2004-299104

A 20041013

JP 2005-113265

A 20050411

AB This invention relates to pharmaceutical comps. for the prevention and treatment of chronic skin diseases, comprising (a) a phosphodiesterase (PDE)-IV inhibitor or a pharmacol. acceptable salt thereof and (b) an immunosuppressant, which are administered simultaneously or sep. with an interval. For example, tablets were formulated containing 2-(3,5-dichloro-4-pyridinyl)-1-(7-methoxyspiro[1,3-benzodioxole-2,1'-cyclopentan]-4-yl)ethanone (PDE-IV inhibitor) 20, tacrolimus (immunosuppressant) 20, lactose 123.4, starch 20, hydroxypropyl cellulose 6, and Mg stearate 0.6 mg per tablet.

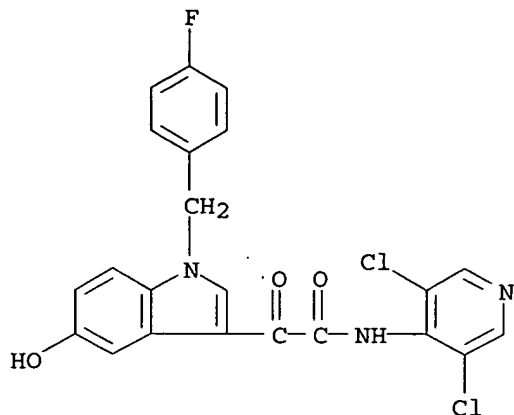
IT 257892-33-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phosphodiesterase IV inhibitor and immunosuppressant combinations for treatment of chronic skin diseases)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 113 THERE ARE 113 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:364924 CAPLUS

DOCUMENT NUMBER: 144:398341

TITLE: Phosphodiesterase IV inhibitor and steroid combinations for the treatment of chronic skin disease
INVENTOR(S): Harada, Daisuke; Kobayashi, Katsuya; Manabe, Haruhiko; Ohshima, Etsuo

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006041121	A1	20060420	WO 2005-JP18855	20051013
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: JP 2004-299103 A 20041013
JP 2005-113264 A 20050411

AB It is intended to provide a remedy and/or a preventive for a chronic skin disease which comprises (a) a phosphodiesterase (PDE)-IV inhibitor or a pharmacol. acceptable salt thereof and (b) a steroid drug, which are administered simultaneously or sep. at an interval. For example, tablets were formulated containing 2-(3,5-dichloro-4-pyridinyl)-1-(7-methoxyspiro[1,3-benzodioxole-2,1'-cyclopentan]-4-yl)ethanone 50, prednisolone 20, lactose

123.4, starch 20, hydroxypropyl cellulose 6, and Mg stearate 0.6 mg per tablet.

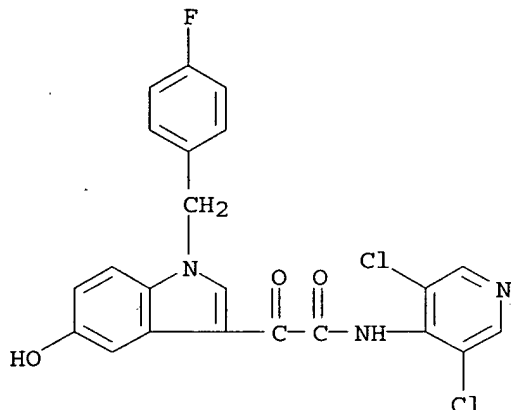
IT 257892-33-4, AWD 12-281

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Usés)

(phosphodiesterase IV inhibitor and steroid combinations for treatment of chronic skin disease)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 128 THERE ARE 128 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:149262 CAPLUS

DOCUMENT NUMBER: 144:239931

TITLE: Pharmaceutical compositions for the treatment of respiratory and gastrointestinal disorders

INVENTOR(S): Jung, Birgit; Himmelsbach, Frank

PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma GmbH & Co. KG

SOURCE: PCT Int. Appl., 321 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006015775	A2	20060216	WO 2005-EP8385	20050803
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM

US 2006035893

A1

20060216

US 2005-189643

20050726

PRIORITY APPLN. INFO.:

EP 2004-18808

A 20040807

OTHER SOURCE(S):

MARPAT 144:239931

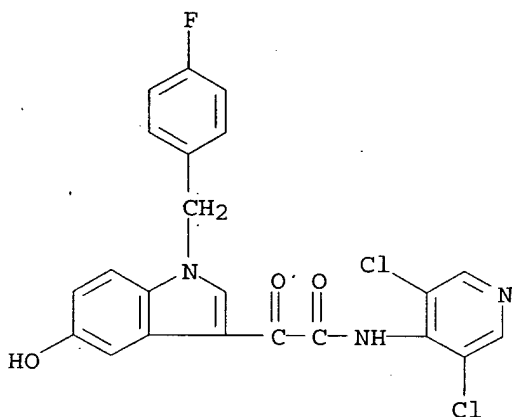
AB The present invention relates to novel pharmaceutical compns. comprising at least 1 EGFR kinase inhibitor and at least one addnl. active compound selected from β -2 mimetics, steroids, PDE-IV inhibitors, p38 MAP kinase inhibitors, NK1 antagonists and endothelin-antagonists, processes for preparing the compns. and the use thereof as drugs in the treatment of respiratory or gastrointestinal complaints, as well as inflammatory diseases of the joints, the skin or the eyes. Thus, an inhalable powder contained an EGFR kinase inhibitor 150, formoterol fumarate dihydrate 50, and lactose 12,300 mg/capsule.

IT 257892-33-4, AWD 12-281

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical compns. for treatment of respiratory and
 gastrointestinal disorders)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:46803 CAPLUS

DOCUMENT NUMBER: 144:135233

TITLE: Pharmaceuticals for inhalation comprising PDE IV inhibitors and glycopyrrolate salts

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Gm.b.H. & Co. K.-G., Germany

SOURCE: Eur. Pat. Appl., 24 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

KIND

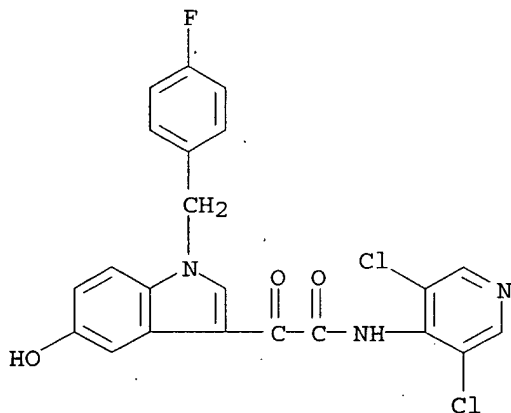
DATE

APPLICATION NO.

DATE

EP 1616567 A1 20060118 EP 2004-16878 20040716
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
 WO 2006008213 A1 20060126 WO 2005-EP52704 20050613
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
 LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
 NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
 SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
 ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF,
 CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM,
 KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG,
 KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2004-16878 A 20040716
 AB The present invention relates to novel pharmaceutical compns. based on PDE
 IV inhibitors and salts of glycopyrrolate salts, processes for preparing them
 and their use in the treatment of respiratory complaints. Thus, a
 formulation contained a glycopyrrolate salt 60, AWD 12281 200, lactose
 12240 µg/capsule.
 IT 257892-33-4, AWD 12-281
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (GW 842470; pharmaceuticals for inhalation comprising PDE IV inhibitors
 and glycopyrrolate salts)
 RN 257892-33-4 CAPLUS
 CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-
 fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)

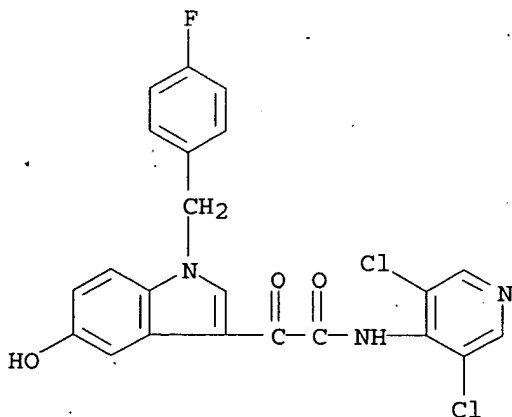


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:1289733 CAPLUS
 DOCUMENT NUMBER: 144:40794
 TITLE: Combinations comprising antimuscarinic agents and PDE4
 inhibitors
 INVENTOR(S): Gras Escardo, Jordi; Llenas Calvo, Jesus; Ryder,
 Hamish; Orviz Diaz, Pio
 PATENT ASSIGNEE(S): Almirall Prodesfarma S.A., Spain

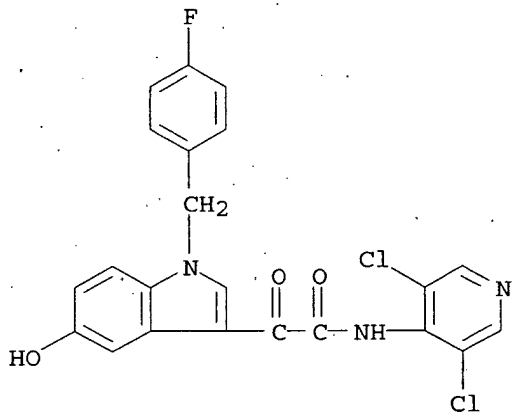
SOURCE: PCT Int. Appl., 43 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005115465	A1	20051208	WO 2005-EP5839	20050531
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005247108	A1	20051208	AU 2005-247108	20050531
CA 2533061	AA	20051208	CA 2005-2533061	20050531
GB 2419819	A1	20060510	GB 2005-26502	20050531
PRIORITY APPLN. INFO.:			ES 2004-1312	A 20040531
			WO 2005-EP1969	A 20050224
			WO 2005-GB722	A 20050225
			WO 2005-GB740	A 20050225
			WO 2005-EP5841	W 20050531
AB A combination which comprises (a) a PDE4 inhibitor and (b) an antagonist of M3 muscarinic receptors which is (3R)-1-phenethyl-3-(9H-xanthene-9-carboxyloxy)-1-azoniabicyclo[2.2.2]octane, in the form of a salt having an anion X, which is a pharmaceutically acceptable anion of a mono or polyvalent acid.				
IT 257892-33-4 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combinations comprising antimuscarinic agents and PDE4 inhibitors)				
RN 257892-33-4 CAPLUS				
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)				



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1267950 CAPLUS
DOCUMENT NUMBER: 144:266281
TITLE: AWD-12-281 (inhaled) Elbion/GlaxoSmithKline
AUTHOR(S): Gutke, Hans-Juergen; Guse, Jan-Hinrich; Khobzaoui, Moussa; Renukappa-Gutke, Thejavathi; Burnet, Michael
CORPORATE SOURCE: Synovo GmbH, Tübingen, D-72076, Germany
SOURCE: Current Opinion in Investigational Drugs (Thomson Scientific) (2005), 6(11), 1149-1158
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: Thomson Scientific
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Elbion (formerly ASTA Medica) and GlaxoSmithKline are developing an inhaled formulation of AWD-12-281 for the potential treatment of chronic obstructive pulmonary disease (COPD). By May 2005, phase II trials of this 5-hydroxyindole PDE4 inhibitor for COPD were ongoing.
IT 257892-33-4, AWD-12-281
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 inhibitor AWD-12-281 was safe and effective in treatment of chronic obstructive pulmonary disease patient)
RN 257892-33-4 CAPLUS
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1155523 CAPLUS
DOCUMENT NUMBER: 143:416252
TITLE: Novel medicament combinations for the treatment of respiratory diseases
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany
SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005239778	A1	20051027	US 2005-109094	20050419
DE 102004019540	A1	20051110	DE 2004-102004019540	20040422
DE 102004052987	A1	20060504	DE 2004-102004052987	20041103
WO 2005102349	A1	20051103	WO 2005-EP4073	20050418

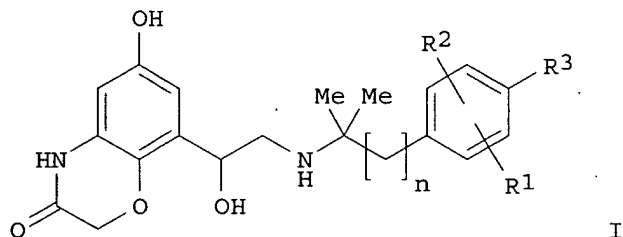
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

DE 2004-102004019540A	20040422
US 2004-578542P	P 20040610
DE 2004-102004052987A	20041103
EP 2005-2496	A 20050207

OTHER SOURCE(S): MARPAT 143:416252
 GI



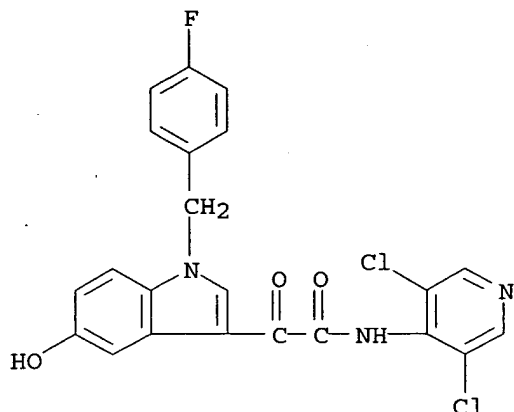
AB The present invention relates to a pharmaceutical composition comprising one or more compds. of formula I wherein n denotes 1 or 2; R1 denotes hydrogen, halogen, C1-C4-alkyl or -O-C1-C4-alkyl; R2 denotes hydrogen, halogen, C1-C4-alkyl or -O-C1-C4-alkyl; R3 denotes C1-C4-alkyl, OH, halogen, -O-C1-C4-alkyl, -O-C1-C4-alkylene-COOH, -O-C1-C4-alkylene-CO-O-C1-C4-alkyl, and at least one other active substance for the treatment of respiratory diseases. The second active substance can be an anticholinergic, a phosphodiesterase IV inhibitor, a steroid, a LTD4 antagonist or an EGFR inhibitor.

IT 257892-33-4, AWD-12-281

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phosphodiesterase IV inhibitor; novel medicament combinations for treatment of respiratory diseases)

RN 257892-33-4 CAPLUS
 CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 8 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:823606 CAPLUS

DOCUMENT NUMBER: 143:206419

TITLE: Treatment of rhinitis with anticholinergics alone or in combination with antihistamines, phosphodiesterase 4 inhibitors, or corticosteroids

INVENTOR(S): Maus, Joachim; Petzold, Ursula; Szelenyi, Istvan; Hoffmann, Torsten; Weingart, Mario

PATENT ASSIGNEE(S): Sofotec G.m.b.H. & Co. K.-G., Germany

SOURCE: PCT Int. Appl., 16 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005074983	A2	20050818	WO 2005-EP653	20050124
WO 2005074983	A3	20060413		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

US 2005222102 A1 20051006 US 2005-51470 20050207

PRIORITY APPLN. INFO.: US 2004-541950P P 20040206

AB The invention provides combinations comprising a topical anticholinergic drug alone or in combination with topically administered antihistamines, topically or orally administered phosphodiesterase 4 inhibitors or topical

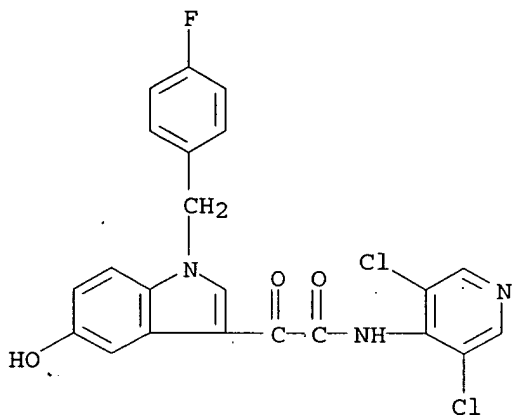
corticosteroids for the treatment of rhinitis of various origins. It further comprises presentation of these combinations in locally applied formulations and includes various pharmaceutical formulations suitable for topical application, e.g. nasal sprays, nasal drops, emulsions, pastes, creams and gels.

IT 257892-33-4, AWD-12-281

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticholinergics alone or in combination with antihistamines, phosphodiesterase 4 inhibitors, or corticosteroids for treatment of rhinitis)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:823578 CAPLUS

DOCUMENT NUMBER: 143:229872

TITLE: Preparation of aminopyri(mi)dinecarboxamide CB2 modulators for use in combination with PDE4 inhibitors for treating pain, immune, inflammatory and rheumatic diseases

INVENTOR(S): Green, Richard Howard; Brown, Andrew James; Connor, Helen Elizabeth; Eatherton, Andrew John; Giblin, Gerard Martin Paul; Jandu, Karamjit Singh; Knowles, Richard Graham; Mitchell, William Leonard; Naylor, Alan; O'Shaughnessy, Celestine Theresa; Palombi, Giovanni; Rawlings, Derek Anthony; Slingsby, Brian Peter; Tralau-Stewart, Catherine Jane; Whittington, Andrew Richard; Williamson, Richard Alexander

PATENT ASSIGNEE(S): Glaxo Group Limited, UK; Doughty, Jennifer Margaret

SOURCE: PCT Int. Appl., 192 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----

WO 2005074939 A1 20050818 WO 2005-GB348 20050201
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

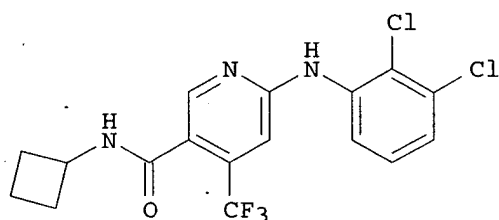
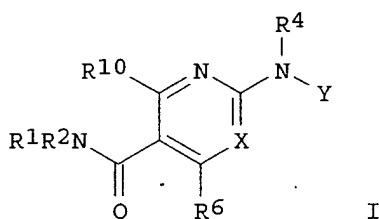
GB 2004-2355

A 20040203

OTHER SOURCE(S):

MARPAT 143:229872

GI



AB The invention is related to combination of one or more CB2 modulators of formula I [X = CH, N; Y = (un)substituted Ph; R1 = H, cyclo/alkyl, (un)substituted haloalkyl; R2 = C(R7)2R3; R3 = (un)substituted non-aromatic heterocyclyl, cycloalk(en)yl, 5-6 membered aromatic heterocyclyl, etc.; R4 = H, COMe, SO2Me, cyclo/alkyl, (un)substituted haloalkyl; R6 = Me, Cl, CHmFn; n = 1-3; m = 0-2; (n + m) = 3; R7 = H, alkyl; when X = CH, R6 = Cl, or (un)substituted alkyl and R10 = H, or R10 = Cl, or (un)substituted alkyl and R10 = H; and their pharmaceutically acceptable salts] and one or more PDE4 inhibitors useful for treating conditions which are mediated by the activity of CB2 receptors or conditions which are mediated by PDE4, such as an immune disorder, an inflammatory disorder, pain, rheumatoid. The invention is also related to the preparation of CB2 modulators I. For example, reacting cyclobutylamine with 6-(2,3-dichlorophenylamino)-4-trifluoromethylnicotinic acid (preparation given) gave II in 81% yield. Selected I had EC50 values of >300 nM but <1000 nM and efficacy value of >50% at the cloned human cannabinoid CB2 receptor. Three formulations are given.

IT 257892-33-4

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG

AU 2004241749 A1 20041202 AU 2004-241749 20040519

CA 2525946 AA 20041202 CA 2004-2525946 20040519

EP 1628682 A2 20060301 EP 2004-766017 20040519

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

US 2006094723 A1 20060504 US 2005-556888 20051115

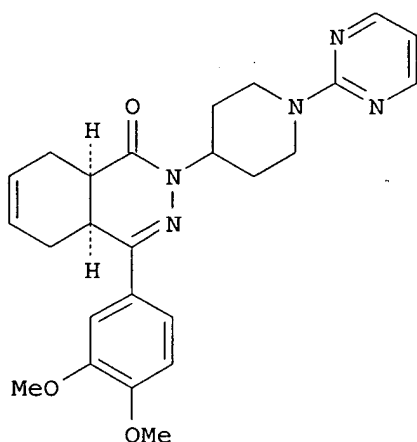
NO 2005005941 A 20051214 NO 2005-5941 20051214

PRIORITY APPLN. INFO.:

EP 2003-11609 A 20030522

WO 2004-EP50869 W 20040519

GI



I

AB The invention relates to the combined administration of a PDE4 inhibitor and a PDE5 inhibitor for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or phosphodiesterase 5 (PDE5) activity is detrimental. Patients were administered orally one tablet of Roflumilase and once daily a tablet of Viagra. An example of another selected PDE4 inhibitor is I.

IT 257892-33-4, AWD-12-281

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (composition comprising a PDE4 inhibitor and a PDE5 inhibitor)

RN 257892-33-4 CAPLUS

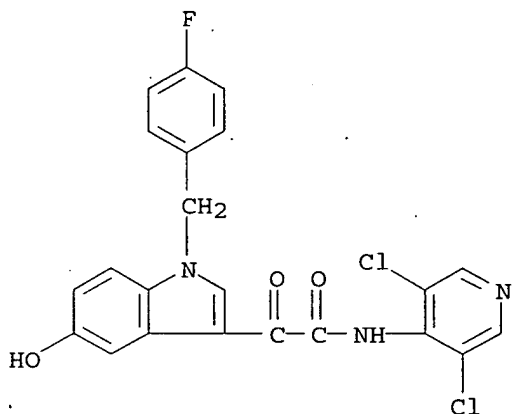
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)

AB A pharmaceutical composition comprises: (a) a compound of formula I wherein X-
is an anion with a single neg. charge; and (b) a PDE IV inhibitor, or an enantiomer, mixture of enantiomers, racemate, solvate, or hydrate thereof. A processes for preparing them, and their use in the treatment of respiratory complaints is also disclosed. A suspension aerosol contained I bromide 0.050, AWD-12-281 0.060, soya lecithin 0.2 and TG 134a: TG 227 (2:3) q.s. 100%.

IT 257892-33-4, AWD-12-281
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments for inhalation comprising anticholinergic and PDE IV inhibitor)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1036929 CAPLUS

DOCUMENT NUMBER: 142:16825

TITLE: Composition comprising a PDE4 inhibitor and a PDE5 inhibitor

INVENTOR(S): Dunkern, Thorsten; Hatzelmann, Armin; Schudt, Christian; Grimminger, Friedrich; Ghofrani, Hossein Ardeschir

PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany

SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

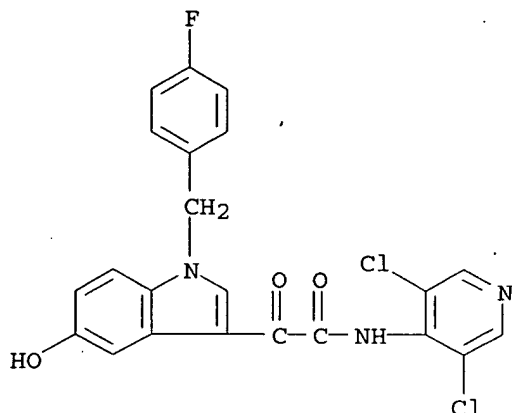
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004103407	A2	20041202	WO 2004-EP50869	20040519
WO 2004103407	A3	20050217		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

(PDE4 inhibitor, combination therapy agent; preparation of aminopyri(mi)dinecarboxamide CB2 modulators for use in combination with PDE4 inhibitors for treating pain, immune, inflammatory and rheumatic diseases)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:735067 CAPLUS

DOCUMENT NUMBER: 143:186747

TITLE: Combination of anticholinergics and inhibitors of phosphodiesterase type 4 for the treatment of respiratory diseases

INVENTOR(S): Maus, Joachim; Cnota, Peter Jurgen; Szelenyi, Istvan; Fyrnys, Beatrix

PATENT ASSIGNEE(S): Sofotec GmbH & Co. Kg, Germany

SOURCE: U.S. Pat. Appl. Publ., 5 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005175547	A1	20050811	US 2005-51463	20050207
WO 2005074982	A2	20050818	WO 2005-EP651	20050124
WO 2005074982	A3	20060406		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,

RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2004-541955P

P 20040206

AB The present invention relates to a combination of an inhaled/oral PDE 4 inhibitor in combination with inhaled anticholinergic bronchodilators (muscarinic receptor antagonists), preferentially roflumilast or AWD-12-281 and R,R-glycopyrrolate, for symptomatic or prophylactic treatment of respiratory diseases, especially those accompanied by obstruction or inflammation such as chronic obstructive pulmonary disease or asthma. It further comprises the presentation of this combination in a locally applied (inhaled) formulation and application in an inhalation device for instance in the Novolizer. The influence of R,R-glycopyrrolate in combination with PDE4 inhibitors on TNF secretion was investigated by using human peripheral blood mononuclear cells. Powder inhalation with 50 µg R,R-glycopyrrolate and 500 µg AWD 12-281 per single dose were prepared

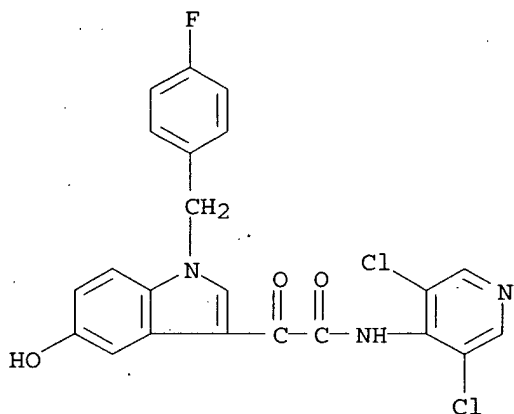
IT 257892-33-4, Awd 12 281

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination of anticholinergics and inhibitors of phosphodiesterase for treatment of respiratory diseases)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:586215 CAPLUS

DOCUMENT NUMBER: 143:120526

TITLE: Pharmaceutical compositions based on anticholinergics and additional active ingredients

INVENTOR(S): Pairet, Michel; Pieper, Michael P.; Meade, Christopher John Montague; Reichl, Richard; Schmelzer, Christel; Jung, Birgit

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. Kg, Germany

SOURCE: U.S. Pat. Appl. Publ., 50 pp., Cont.-in-part of U.S. Ser. No. 824,391.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005148562	A1	20050707	US 2004-6940	20041208
DE 10062712	A1	20020620	DE 2000-10062712	20001215
DE 10063957	A1	20020627	DE 2000-10063957	20001220
DE 10110772	A1	20020912	DE 2001-10110772	20010307
DE 10111058	A1	20020912	DE 2001-10111058	20010308
DE 10113366	A1	20020926	DE 2001-10113366	20010320
DE 10138272	A1	20030227	DE 2001-10138272	20010810
US 2002151541	A1	20021017	US 2001-7182	20011019
US 2002183292	A1	20021205	US 2001-86145	20011019
US 2002137764	A1	20020926	US 2001-40196	20011025
US 2002122773	A1	20020905	US 2001-27662	20011220
DE 10206505	A1	20030828	DE 2002-10206505	20020216
US 2002169181	A1	20021114	US 2002-92116	20020306
US 6620438	B2	20030916		
US 2002193393	A1	20021219	US 2002-93240	20020307
US 2002183347	A1	20021205	US 2002-100659	20020318
US 6608054	B2	20030819		
US 2003158196	A1	20030821	US 2003-360064	20030207
US 2003181478	A1	20030925	US 2003-395777	20030324
US 6890517	B2	20050510		
US 2003203925	A1	20031030	US 2003-413065	20030414
US 2003212075	A1	20031113	US 2003-419358	20030421
US 6696042	B2	20040224		
US 2004024007	A1	20040205	US 2003-613783	20030703
US 2004151770	A1	20040805	US 2004-763894	20040123
US 2004161386	A1	20040819	US 2004-775901	20040210
US 2004176338	A1	20040909	US 2004-776757	20040211
US 2004192675	A1	20040930	US 2004-824391	20040414
US 2005147564	A1	20050707	US 2005-68134	20050228
PRIORITY APPLN. INFO.:			DE 2000-10054042	A 20001031
			US 2000-253613P	P 20001128
			DE 2000-10062712	A 20001215
			DE 2000-10063957	A 20001220
			US 2000-257220P	P 20001221
			US 2000-257221P	P 20001221
			DE 2001-10110772	A 20010307
			DE 2001-10111058	A 20010308
			DE 2001-10113366	A 20010320
			US 2001-281653P	P 20010405
			US 2001-281857P	P 20010405
			US 2001-281874P	P 20010405
			DE 2001-10138272	A 20010810
			US 2001-314599P	P 20010824
			US 2001-7182	B1 20011019
			US 2001-86145	B1 20011019
			US 2001-27662	B1 20011220
			DE 2002-10206505	A 20020216
			US 2002-92116	A1 20020306
			US 2002-93240	B1 20020307
			US 2002-100659	A1 20020318
			US 2002-369213P	P 20020401
			US 2003-360064	A2 20030207
			US 2003-413065	B2 20030414
			US 2003-419358	A1 20030421
			US 2003-613783	A2 20030703

US 2004-763894	A2 20040123
US 2004-775901	A2 20040210
US 2004-776757	A2 20040211
US 2004-824391	A2 20040414
US 2001-40196	B1 20011025
US 2003-395777	A1 20030324

OTHER SOURCE(S): MARPAT 143:120526

AB A pharmaceutical composition comprising an anticholinergic and at least one addnl. active ingredient selected from among corticosteroids, dopamine agonists, PDE-IV inhibitors, NK1-antagonists, endothelin antagonists, antihistamines, and EGFR-kinase inhibitors, processes for preparing them and their use in the treatment of respiratory diseases. Among a number of compds. prepared was N-[2-[3,5-bis(trifluoromethyl)phenyl]ethyl]-2-[4-[(3-hydroxypropyl)methylamino]piperidin-1-yl]-N-methyl-2-phenylacetamide. Inhalable powders include a formulation containing tiotropium bromide, budesonide, and lactose.

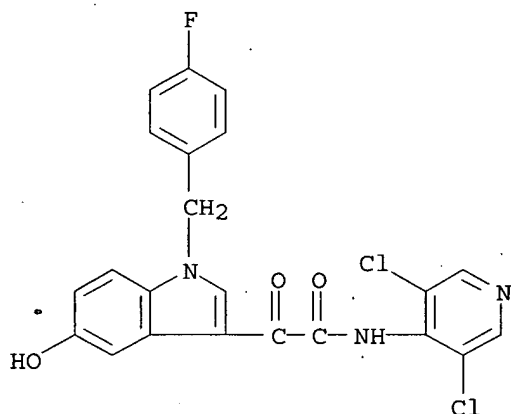
IT 257892-33-4, AWd-12-281

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical compns. based on anticholinergics and addnl. active ingredients)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:136543 CAPLUS

DOCUMENT NUMBER: 142:246142

TITLE: Medicaments comprising PDE IV inhibitors and an anticholinergic agent for treating respiratory disorders

INVENTOR(S): Germeyer, Sabine; Meade, Christopher John Montague; Meissner, Helmut; Morschhaeuser, Gerd; Pairet, Michel; Pestel, Sabine; Pieper, Michael P.; Pohl, Gerald; Reichl, Richard; Speck, Georg

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

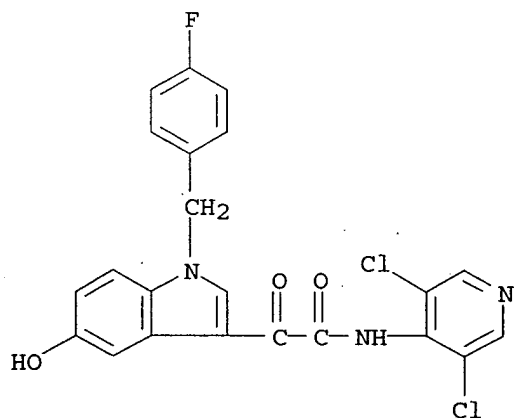
SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005013967	A1	20050217	WO 2004-EP8003	20040723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005043343	A1	20050224	US 2004-891562	20040715
CA 2533786	AA	20050217	CA 2004-2533786	20040723
EP 1651208	A1	20060503	EP 2004-741118	20040723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
PRIORITY APPLN. INFO.:			EP 2003-17039	A 20030728
			US 2003-508119P	P 20031002
			WO 2004-EP8003	W 20040723
OTHER SOURCE(S): MARPAT 142:246142				
AB The present invention relates to pharmaceutical compns. based on PDE IV inhibitors and salts of a novel anticholinergic, processes for preparing them and their use in the treatment of respiratory complaints. For example, scopine 9-methylfluorene-9-carboxylate methobromide was prepared and formulated into inhalable powder containing the drug 80 µg, AWD-12-281 200 µg, and lactose 12220 µg per capsule.				
IT 257892-33-4, AWD 12-281 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (GW-842470; inhalable compns. comprising anticholinergic agent and PDE IV inhibitors for treating respiratory disorders)				
RN 257892-33-4 CAPLUS CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)				



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:99152 CAPLUS

DOCUMENT NUMBER: 142:204737

TITLE: Medicaments for inhalation comprising an anticholinergic and a PDE IV inhibitor

INVENTOR(S): Meade, Christopher John Montague; Pairet, Michel; Pieper, Michel; Pieper, Michael P.

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany

SOURCE: U.S. Pat. Appl. Publ., 18 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

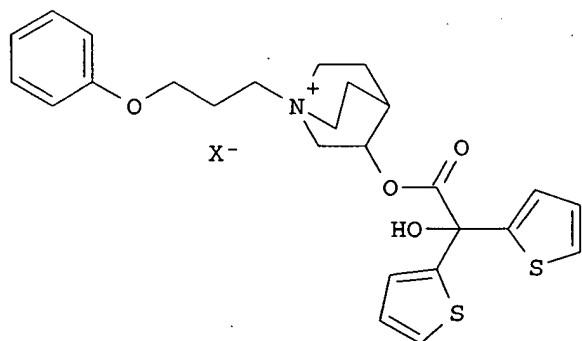
FAMILY ACC. NUM. COUNT: 1

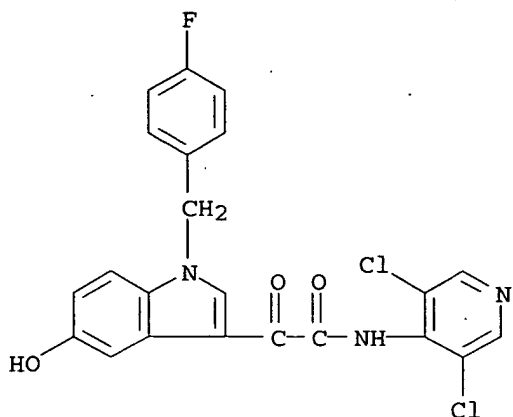
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005026886	A1	20050203	US 2004-891551	20040715
CA 2534125	AA	20050217	CA 2004-2534125	20040717
WO 2005013993	A1	20050217	WO 2004-EP8024	20040717
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1651222	A1	20060503	EP 2004-741128	20040717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
PRIORITY APPLN. INFO.:			EP 2003-17164	A 20030729
			US 2003-508125P	P 20031002
			WO 2004-EP8024	W 20040717

OTHER SOURCE(S): MARPAT 142:204737

GI





L25 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:996001 CAPLUS

DOCUMENT NUMBER: 141:406065.

TITLE: Composition comprising a PDE-4 inhibitor and a TNF-alpha antagonist

INVENTOR(S): Barsig, Johannes; Weimar, Christian

PATENT ASSIGNEE(S): Altana Pharma AG, Germany

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098633	A1	20041118	WO 2004-EP50748	20040510
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-10581 A 20030512

AB The invention relates to the combined administration of a PDE4 inhibitor and a TNF α antagonist selected from the group consisting of etanercept, onercept and pegsunercept for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or tumor necrosis factor alpha (TNF α) activity is detrimental.

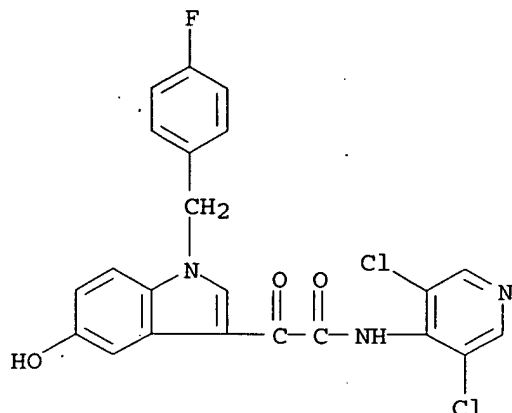
IT 257892-33-4, AWD 12-281

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic activity of phosphodiesterase 4 inhibitors and TNF α antagonists)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-

fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:995979 CAPLUS

DOCUMENT NUMBER: 141:406064

TITLE: Composition comprising a PDE4 inhibitor and soluble human Type II interleukin-1 receptor (shuIL-1RII) for disease therapy

INVENTOR(S): Barsig, Johannes

PATENT ASSIGNEE(S): Altana Pharma AG, Germany

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098606	A1	20041118	WO 2004-EP50749	20040510
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-10596 A 20030512

AB The invention relates to the combined administration of a PDE4 inhibitor and shuIL-1R II for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or interleukin-1 (IL-1) activity is detrimental.

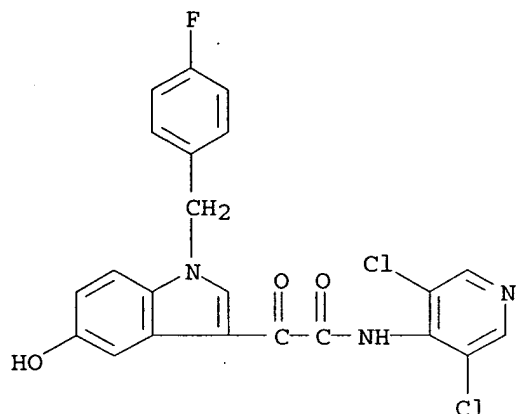
IT 257892-33-4, AWD 12-281

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(composition comprising a PDE4 inhibitor and soluble human Type II interleukin-1 receptor (shuIL-1RII) for disease therapy)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:995978 CAPLUS

DOCUMENT NUMBER: 141:406063

TITLE: Pharmaceutical composition comprising a PDE4 inhibitor and IL-1 trap for treatment of disease

INVENTOR(S): Barsig, Johannes

PATENT ASSIGNEE(S): Altana Pharma AG, Germany

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

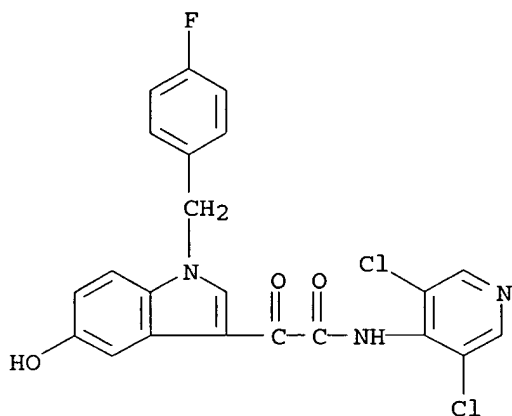
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098605	A1	20041118	WO 2004-EP50747	20040510
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2003-10631 A 20030512

AB The invention relates to the combined administration of a PDE4 inhibitor and IL-1 Trap for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or interleukin-1 (IL-1) activity is detrimental.

IT 257892-33-4, AWD 12-281
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (pharmaceutical composition comprising a PDE4 inhibitor and IL-1 trap for
 treatment of disease)
 RN 257892-33-4 CAPLUS
 CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-
 fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 18 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:610086 CAPLUS

DOCUMENT NUMBER: 141:134069

TITLE: PDE4 inhibitors for the treatment of neoplasms of
 lymphoid cells

INVENTOR(S): Hatzelmann, Armin; Tenor, Hermann; Gekeler, Volker;
 Sanders, Karl; Garattini, Enrico; Braunger, Juergen;
 Schudt, Christian

PATENT ASSIGNEE(S): Altana Pharma Ag, Germany

SOURCE: PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004062671	A2	20040729	WO 2004-EP196	20040114
WO 2004062671	A3	20050127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ				
AU 2004204355	A1	20040729	AU 2004-204355	20040114
CA 2512819	AA	20040729	CA 2004-2512819	20040114
EP 1587512	A2	20051026	EP 2004-701902	20040114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: EP 2003-787 A 20030114
WO 2004-EP196 W 20040114

OTHER SOURCE(S): MARPAT 141:134069

AB The invention relates to the use of certain PDE4 inhibitors alone or in combination with one or more differentiation inducing agents and/or an agent effective in raising intracellular concns. of cAMP or a stable analog of cAMP in the preparation of pharmaceutical compns. for the treatment of neoplasms of lymphoid cells.

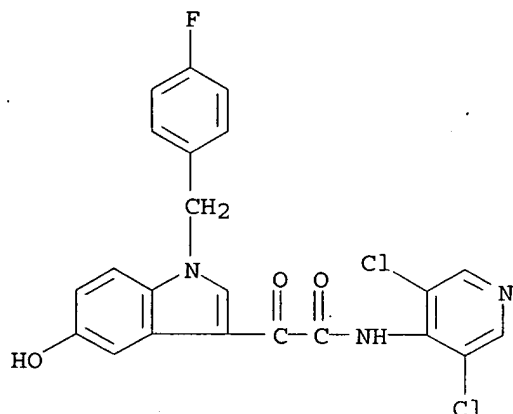
IT 257892-33-4, AWD-12-281

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phosphodiesterase 4 (PDE4) inhibitors for treatment of neoplasms of lymphoid cells in combination with differentiation inducers and agents that increase cAMP levels or cAMP analogs)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 19 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:467725 CAPLUS

DOCUMENT NUMBER: 141:17651

TITLE: Phosphodiesterase IV and phosphodiesterase III/IV inhibitors for use in the treatment of cachexia

INVENTOR(S): Schmidt, Mathias

PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

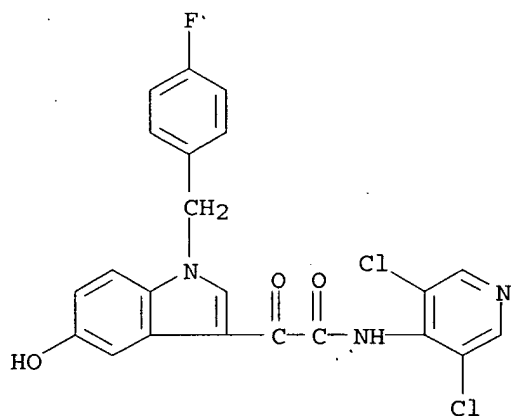
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004047817	A1	20040610	WO 2003-EP13313	20031126
W:	AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, EG, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW			
RW:	AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,			

SI, SK, TR
 CA 2506949 AA 20040610 CA 2003-2506949 20031126
 AU 2003289898 A1 20040618 AU 2003-289898 20031126
 EP 1567136 A1 20050831 EP 2003-782232 20031126
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 JP 2006508996 T2 20060316 JP 2004-554493 20031126
 US 2006079540 A1 20060413 US 2005-535815 20050520
 PRIORITY APPLN. INFO.: EP 2002-26548 A 20021127
 WO 2003-EP13313 W 20031126
 AB The invention discloses the use of a PDE IV or PDE III/IV inhibitor for
 the treatment of cachexia.
 IT 257892-33-4
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (phosphodiesterase IV and phosphodiesterase III/IV inhibitors for
 treatment of cachexia)
 RN 257892-33-4 CAPLUS
 CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-
 fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:203704 CAPLUS

DOCUMENT NUMBER: 140:229455

TITLE: Combination of glucocorticoids and PDE-4-inhibitors
 for treating respiratory diseases, allergic diseases,
 asthma and COPD

INVENTOR(S): Locher, Mathias; Hermann, Robert

PATENT ASSIGNEE(S): Viatris G.m.b.H. & Co. K.-G., Germany

SOURCE: PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----

WO 2004019984 A1 20040311 WO 2003-EP8607 20030804
W: AU, BR, CA, CN, CO, CZ, GE, HR, ID, IL, IN, JP, KR, LT, LV, MD, MK, MX, NO, NZ, PL, SG, UA, US, UZ, YU, ZA
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

CA 2492645 AA 20040311 CA 2003-2492645 20030804
AU 2003255365 A1 20040319 AU 2003-255365 20030804
EP 1526870 A1 20050504 EP 2003-790851 20030804
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR, BG, CZ, EE, HU, SK

JP 2005539042 T2 20051222 JP 2004-531853 20030804
US 2005288265 A1 20051229 US 2005-523802 20050209
NO 2005001212 A 20050308 NO 2005-1212 20050308

PRIORITY APPLN. INFO.: DE 2002-10236688 A 20020809
WO 2003-EP8607 W 20030804

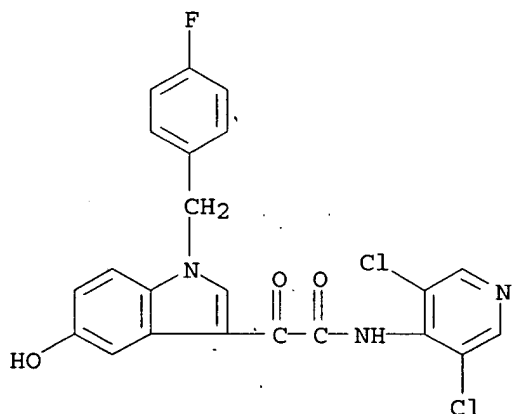
AB The invention relates to a novel combination of a glucocorticoid, especially loteprednol, and at least one phosphodiesterase-4 inhibitor (PDE-4-inhibitor), especially hydroxyindole-derivative

N-(3,5-dichloropyridine-4-yl)-2-[1-(4-fluorbenzyl)-5-hydroxyindole-3-yl]-2-oxoacetamide, for a simultaneous, sequential or sep. administration in the treatment of respiratory diseases, allergic diseases, asthma and chronic obstructive pulmonary diseases (COPD). Formulation of glucocorticoids and PDE-4-inhibitors can be prepared sep. and applied at the same time or at different times during the day; also combinations can be formulated.

IT 257892-33-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of glucocorticoids and PDE-4-inhibitors for treating respiratory diseases, allergic diseases, asthma and COPD)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)

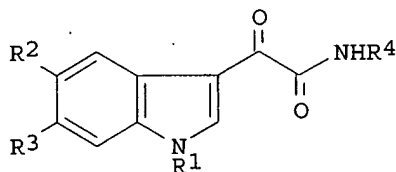


REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:120846 CAPLUS
DOCUMENT NUMBER: 140:163707

TITLE: Method for producing highly pure hydroxyindolylglyoxylic acid amides
 INVENTOR(S): Jaensch, Hans-Joachim; Hartenhauer, Helge; Stange, Hans; Hoefgen, Norbert; Schaefer, Juergen
 PATENT ASSIGNEE(S): Elbion AG, Germany
 SOURCE: PCT Int. Appl., 32 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013127	A1	20040212	WO 2003-EP8500	20030731
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2493982	AA	20040212	CA 2003-2493982	20030731
AU 2003255341	A1	20040223	AU 2003-255341	20030731
US 2004063939	A1	20040401	US 2003-631475	20030731
EP 1525197	A1	20050427	EP 2003-766389	20030731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013467	A	20050705	BR 2003-13467	20030731
CN 1671692	A	20050921	CN 2003-818537	20030731
JP 2006503002	T2	20060126	JP 2004-525409	20030731
NO 2005001086	A	20050502	NO 2005-1086	20050228
PRIORITY APPLN. INFO.:			US 2002-400236P	P 20020801
			WO 2003-EP8500	W 20030731
OTHER SOURCE(S):			CASREACT 140:163707; MARPAT 140:163707	
GI				

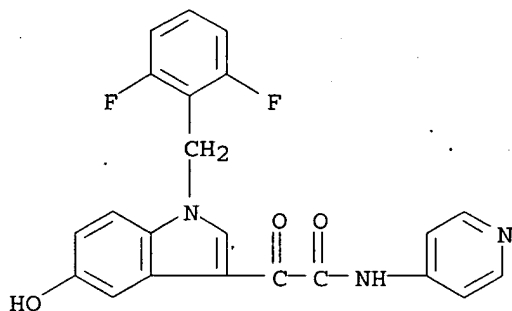


I

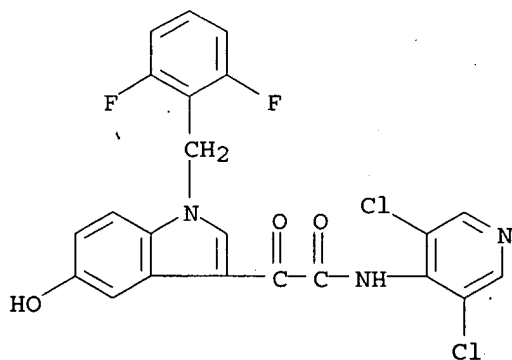
AB The invention relates to a method for producing hydroxyindolylglyoxylic acid amides I [R1 = (un)branched, (un)saturated C1-6-alkyl, 3- to 14-membered mono-, bi- or tricyclic, (un)substituted 5- to 15-membered heterocycle (1 - 6 heteroatoms - N, O, S); R2, R3 = H, OH (one or both OH); R4 = (un)substituted mono- or polycyclic aromatic C6-14-carbocycle, 5 to 15-membered heterocycle (containing N, O, S)] in high yields and in a particularly pure form from 5- or 6-benzyloxyindole or

5,6-di(benzyloxy)indole compds. The method comprises: (a) reaction of 5- or 6-benzyloxyindole or 5,6-di(benzyloxy)indole with R1X (X = halogen); (b) C-acylation of the 1-substituted indole with (COX)2; (c) reaction of the [indol-3-yl]glyoxyl halide with NH3, NH2R4, NH(R4)2; and (d) hydrogenolytic debenzylation. Thus, AWD 12-281 [I; R1 = CH2C6H4F-4, R2 = OH, R3 = H, R4 = 3,5-dichloro-4-pyridyl] was prepared from 5-(benzyloxy)indole via N-benylation with 4-FC6H4CH2Cl, C-acylation with (COCl)2, amidation with 4-amino-3,5-dichloropyridine, and hydrogenolytic debenzylation of I [R1 = CH2C6H4F-4, R2 = OCH2Ph, R3 = H, R4 = 3,5-dichloro-4-pyridyl].

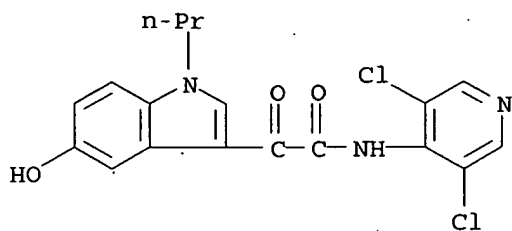
IT 247584-23-2P 247584-24-3P 247584-26-5P
 247584-27-6P 247584-28-7P 247584-29-8P
 247584-30-1P 247584-31-2P 247584-32-3P
 257892-33-4P, AWD 12-281 656237-82-0P
 RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
 (preparation of highly pure hydroxyindolyglyoxylic acid amides)
 RN 247584-23-2 CAPLUS
 CN 1H-Indole-3-acetamide, 1-[(2,6-difluorophenyl)methyl]-5-hydroxy- α -oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



RN 247584-24-3 CAPLUS
 CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(2,6-difluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)

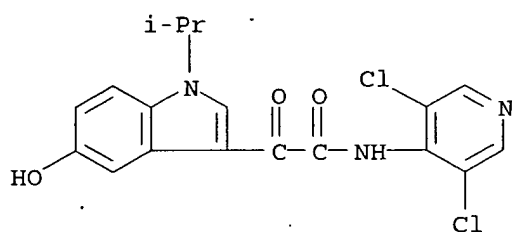


RN 247584-26-5 CAPLUS
 CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-hydroxy- α -oxo-1-propyl- (9CI) (CA INDEX NAME)



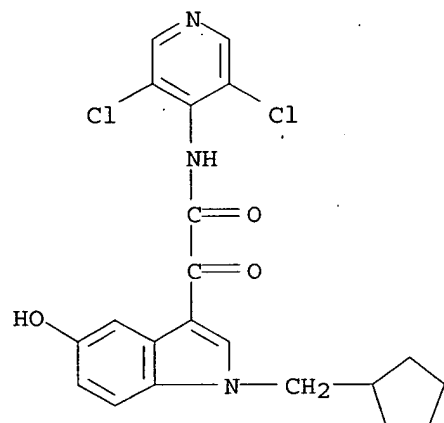
RN 247584-27-6 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-1-(1-methylethyl)-α-oxo- (9CI) (CA INDEX NAME)



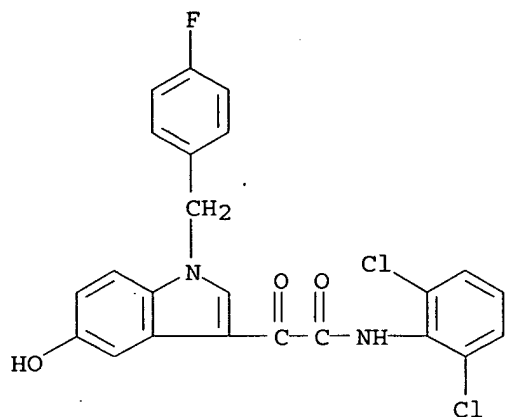
RN 247584-28-7 CAPLUS

CN 1H-Indole-3-acetamide, 1-(cyclopentylmethyl)-N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



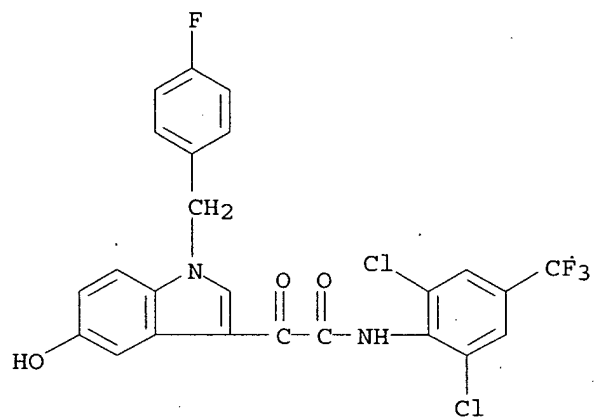
RN 247584-29-8 CAPLUS

CN 1H-Indole-3-acetamide, N-(2,6-dichlorophenyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



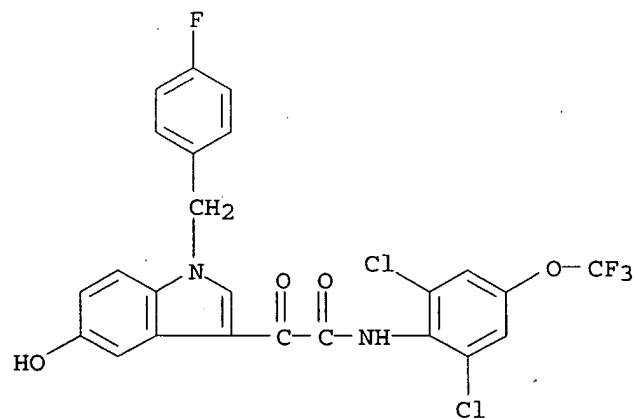
RN 247584-30-1 CAPLUS

CN 1H-Indole-3-acetamide, N-[2,6-dichloro-4-(trifluoromethyl)phenyl]-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)

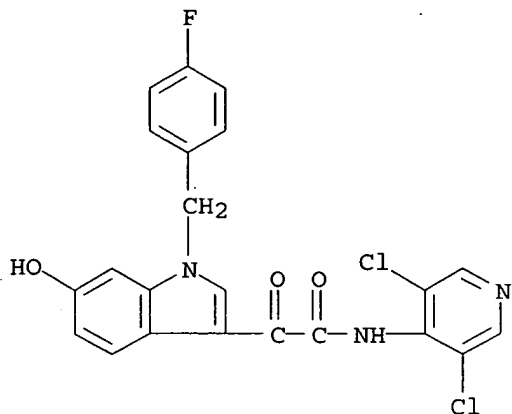


RN 247584-31-2 CAPLUS

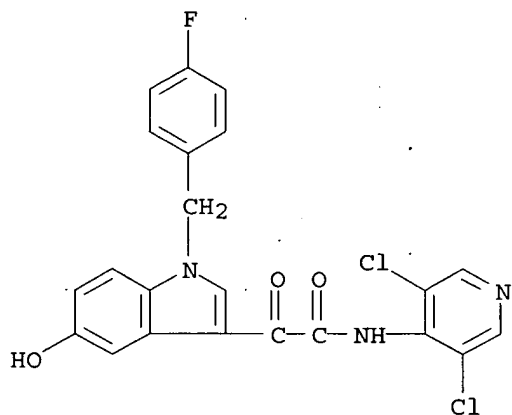
CN 1H-Indole-3-acetamide, N-[2,6-dichloro-4-(trifluoromethoxy)phenyl]-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



RN 247584-32-3 CAPLUS

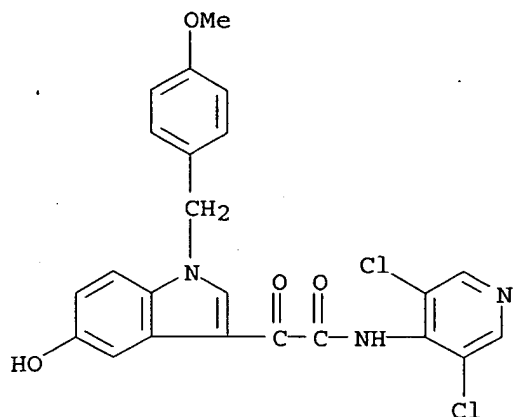
CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-6-hydroxy- α -oxo- (9CI) (CA INDEX NAME)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)

RN 656237-82-0 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-5-hydroxy-1-[(4-methoxyphenyl)methyl]- α -oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:41257 CAPLUS
 DOCUMENT NUMBER: 140:87709
 TITLE: Pharmaceutical compositions comprising anticholinergic agents and phosphodiesterase IV (PDE-IV) inhibitors for the treatment of respiratory diseases
 INVENTOR(S): Pairet, Michel; Meade, Christopher John Montague; Pieper, Michael P.
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
 SOURCE: PCT Int. Appl., 37 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004704	A1	20040115	WO 2003-EP6668	20030625
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10230769	A1	20040122	DE 2002-10230769	20020709
CA 2492026	AA	20040115	CA 2003-2492026	20030625
AU 2003242755	A1	20040123	AU 2003-242755	20030625
EP 1521576	A1	20050413	EP 2003-762509	20030625
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2005532379	T2	20051027	JP 2004-518566	20030625
US 2004058950	A1	20040325	US 2003-614365	20030707
PRIORITY APPLN. INFO.:			DE 2002-10230769	A 20020709
			US 2002-407895P	P 20020903
			WO 2003-EP6668	W 20030625

OTHER SOURCE(S): MARPAT 140:87709

AB The invention provides pharmaceutical compns. comprising anticholinergic agents and PDE-IV inhibitors, as well as a method for the production and use thereof in the treatment of respiratory diseases. Powder inhalant formulations are included.

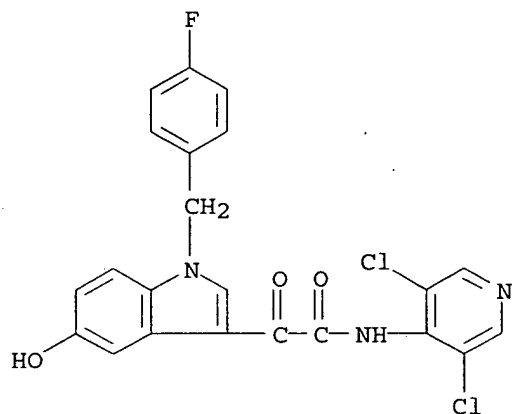
IT 257892-33-4, AWD-12-281 645337-16-2

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical compns. comprising anticholinergic agents and phosphodiesterase IV inhibitors for treatment of respiratory diseases)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



RN 645337-16-2 CAPLUS

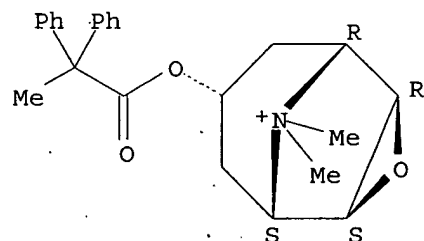
CN 3-Oxa-9-azoniatricyclo[3.3.1.0^{2,4}]nonane, 9,9-dimethyl-7-(1-oxo-2,2-diphenylpropoxy)-, bromide, (1 α ,2 β ,4 β ,5 α ,7 β)-, mixt. with N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo-1H-indole-3-acetamide (9CI) (CA INDEX NAME)

CM 1

CRN 412046-80-1

CMF C24 H28 N O3 . Br

Relative stereochemistry.

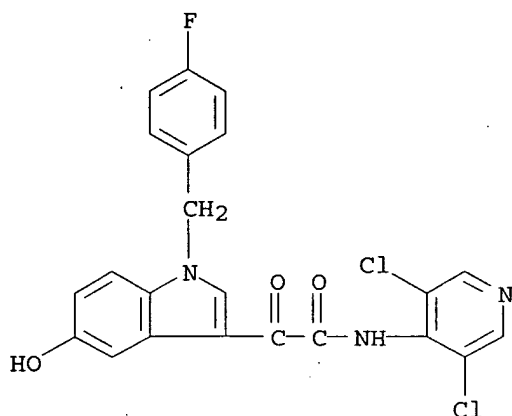


● Br⁻

CM 2

CRN 257892-33-4

CMF C22 H14 Cl2 F N3 O3



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 23 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:719308 CAPLUS

DOCUMENT NUMBER: 139:240373

TITLE: Pharmaceutical composition of a phosphodiesterase 4 (PDE4) inhibitor or a PDE3/4 inhibitor and a histamine receptor antagonist for the treatment of respiratory diseases

INVENTOR(S): Beume, Rolf; Bundschuh, Daniela; Weimar, Christian; Wollin, Stefan-lutz

PATENT ASSIGNEE(S): Altana Pharma Ag, Germany

SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074055	A1	20030912	WO 2003-EP1876	20030225
W: AE, AL, AU, BA, BR, CA, CN, CO, CU, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				
CA 2478612	AA	20030912	CA 2003-2478612	20030225
AU 2003212268	A1	20030916	AU 2003-212268	20030225
EP 1482938	A1	20041208	EP 2003-708130	20030225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008220	A	20050104	BR 2003-8220	20030225

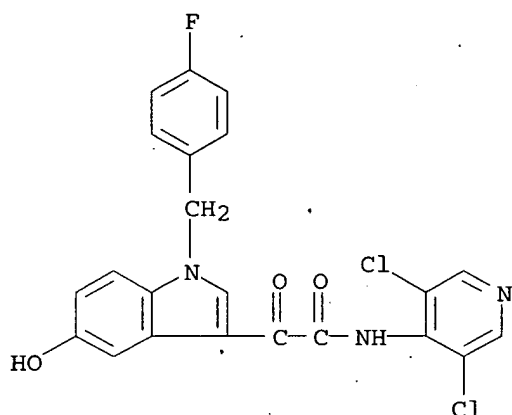
US 2005112069 A1 20050526 US 2003-506875 20030225
 JP 2005524666 T2 20050818 JP 2003-572572 20030225
 NO 2004004230 A 20041206 NO 2004-4230 20041006
 PRIORITY APPLN. INFO.: EP 2002-4987 A 20020306
 WO 2003-EP1876 W 20030225

AB The invention discloses the combined administration of PDE4 or PDE3/4 inhibitors and histamine receptor antagonists for the treatment of respiratory diseases.

IT 257892-33-4, AWD 12-281
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (phosphodiesterase 4 (PDE4) inhibitor or PDE3/4 inhibitor combination with histamine receptor antagonist for treatment of respiratory disease)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)

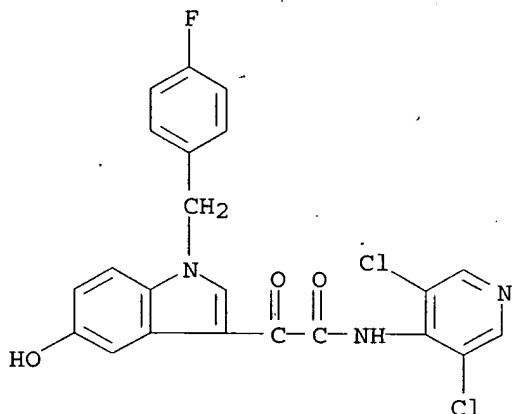


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:376393 CAPLUS
 DOCUMENT NUMBER: 138:379220
 TITLE: Combination of type 4 phosphodiesterase inhibitor and disease-modifying anti-rheumatic drug for treating rheumatoid arthritis
 INVENTOR(S): Barsig, Johannes
 PATENT ASSIGNEE(S): Germany
 SOURCE: U.S. Pat. Appl. Publ., 13 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003092706	A1	20030515	US 2002-184068	20020628
CA 2399840	AA	20030509	CA 2002-2399840	20020827
WO 2003039552	A1	20030515	WO 2002-EP12415	20021107

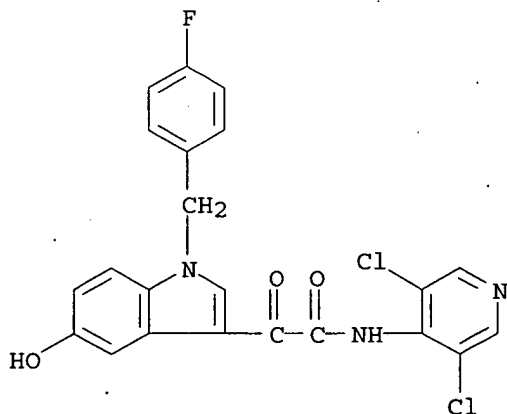
W: AE, AL, BA, BR, CN, CO, CU, DZ, EC, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, TN, UA, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR
 EP 1448202 A1 20040825 EP 2002-792742 20021107
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
 JP 2005508983 T2 20050407 JP 2003-541843 20021107
 PRIORITY APPLN. INFO.: EP 2001-607 A 20011109
 WO 2002-EP12415 W 20021107
 AB The invention relates to the combined administration of a PDE4 or PDE3/4 inhibitor and a disease modifying anti-rheumatic drug (DMARDs) or anti-rheumatic or anti-arthritic drug. Oral treatments with Roflumilast plus methotrexate or Pumafentrine HCl plus methotrexate had additive beneficial effects in delaying the onset and reducing the severity of collagen-induced arthritis in DBA/1 mice.
 IT 257892-33-4, AWD-12-281
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (PDE4 or PDE3/4 inhibitor; combination of phosphodiesterase 4 inhibitor and disease-modifying anti-rheumatic drug for treating rheumatoid arthritis)
 RN 257892-33-4 CAPLUS
 CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:242192 CAPLUS
 DOCUMENT NUMBER: 138:248511
 TITLE: Combination of phosphodiesterase 4 inhibitor and nonsteroidal antiinflammatory drug in treatment of inflammation
 INVENTOR(S): Hatzelmann, Armin; Eltze, Manfred; Klein, Thomas; Kley, Hans-Peter
 PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
 SOURCE: PCT Int. Appl., 42 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English

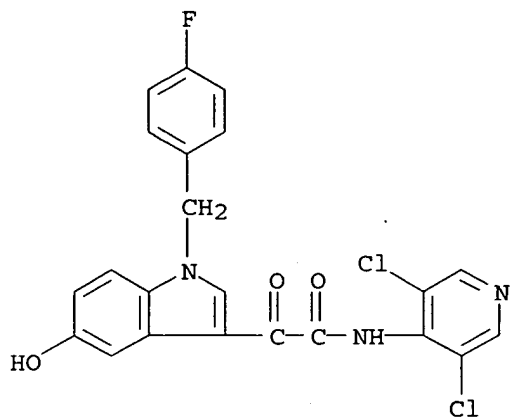
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024489	A2	20030327	WO 2002-EP10424	20020917
WO 2003024489	A3	20030918		
W: AE, AL, AU, BA, BR, CA, CN, CO, CU, DZ, EC, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
CA 2459757	AA	20030327	CA 2002-2459757	20020917
EP 1429807	A2	20040623	EP 2002-772313	20020917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002012606	A	20040817	BR 2002-12606	20020917
JP 2005504077	T2	20050210	JP 2003-528583	20020917
CN 1625411	A	20050608	CN 2002-818241	20020917
US 2004242597	A1	20041202	US 2004-489920	20040318
ZA 2004002654	A	20050214	ZA 2004-2654	20040405
NO 2004001596	A	20040618	NO 2004-1596	20040419
PRIORITY APPLN. INFO.:			EP 2001-473	A 20010919
			WO 2002-EP10424	W 20020917
AB	The invention relates to the combined administration of PDE4-inhibitors and NSAIDs for the treatment of an inflammatory disease and/or an inflammation associated disorder while minimizing gastrointestinal side effects, such as gastric erosions and ulcer, which are frequently associated with the use of NSAIDs. PDE4 inhibitors Rolipram, Roflumilast, and RP73401 inhibited or prevented diclofenac induced gastrointestinal bleeding in mice.			
IT	257892-33-4, AWD 12-281 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (phosphodiesterase inhibitor; combination of phosphodiesterase 4 inhibitor and nonsteroidal antiinflammatory drug in treatment of inflammation)			
RN	257892-33-4 CAPLUS			
CN	1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)			



L25 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:242191 CAPLUS
 DOCUMENT NUMBER: 138:248522
 TITLE: Combined administration of phosphodiesterase PDE4 or
 PDE3/4 inhibitors and leukotriene receptor antagonists
 for the treatment of respiratory tract disorders
 INVENTOR(S): Beume, Rolf; Bundschuh, Daniela; Weimar, Christian;
 Wollin, Stefan-Lutz
 PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
 SOURCE: PCT Int. Appl., 40 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024488	A2	20030327	WO 2002-EP10423	20020917
WO 2003024488	A3	20030904		
W:	AE, AL, AU, BA, BR, CA, CN, CO, CU, DZ, EC, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, TN, UA, US, VN, YU, ZA, ZW			
RW:	AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR			
CA 2460442	AA	20030327	CA 2002-2460442	20020917
EP 1429843	A2	20040623	EP 2002-798730	20020917
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
BR 2002012582	A	20041013	BR 2002-12582	20020917
JP 2005505570	T2	20050224	JP 2003-528582	20020917
CN 1655846	A	20050817	CN 2002-818260	20020917
ZA 2004002653	A	20050214	ZA 2004-2653	20040405
NO 2004001595	A	20040616	NO 2004-1595	20040419
US 2005014762	A1	20050120	US 2004-489903	20040818
PRIORITY APPLN. INFO.:			EP 2001-474	A 20010919
			WO 2002-EP10423	W 20020917
AB	The invention relates to the combined administration of PDE4 or PDE3/4 inhibitors and leukotriene receptor antagonists for the treatment of respiratory tract disorders. The inhibitory effects of Roflumilast and Montelukast sodium salt on SRS-A-induced bronchoconstriction were additive in guinea pigs.			
IT	257892-33-4 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (phosphodiesterase inhibitor; combined administration of phosphodiesterase PDE4 or PDE3/4 inhibitors and leukotriene receptor antagonists for treatment of respiratory tract disorders)			
RN	257892-33-4 CAPLUS			
CN	1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)			



L25 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:5806 CAPLUS
 DOCUMENT NUMBER: 138:78456
 TITLE: Composition comprising a PDE-4 inhibitor and
 H1-receptor antagonist for treatment of respiratory
 diseases
 INVENTOR(S): Knowles, Richard Graham; Ward, Peter; Nials, Anthony
 Terence
 PATENT ASSIGNEE(S): Glaxo Group Limited, UK
 SOURCE: PCT Int. Appl., 18 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000289	A1	20030103	WO 2002-GB2679	20020617
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2450758	AA	20030103	CA 2002-2450758	20020617
EP 1404369	A1	20040407	EP 2002-735611	20020617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1518460	A	20040804	CN 2002-812473	20020617
BR 2002010473	A	20040810	BR 2002-10473	20020617
JP 2005501023	T2	20050113	JP 2003-506932	20020617
US 2004176419	A1	20040909	US 2003-480969	20031208
ZA 2003009587	A	20050117	ZA 2003-9587	20031210
PRIORITY APPLN. INFO.:			GB 2001-15181	A 20010620
			WO 2002-GB2679	W 20020617
AB A method of prophylaxis, treating, or reducing the duration or frequency of the exacerbations associated with a respiratory disease, such as chronic				

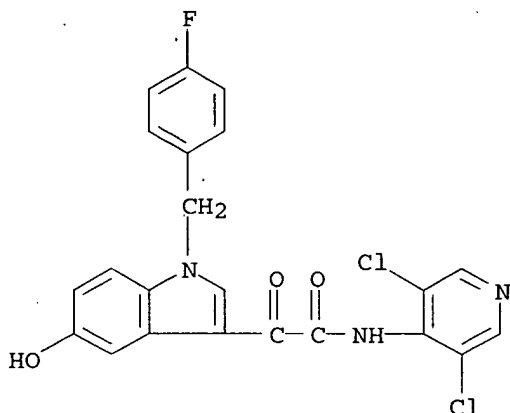
obstructive pulmonary disease or asthma, comprises administering to a patient an effective amount of a phosphodiesterase-4 (PDE-4) inhibitor, e.g., cilomilast, in combination with an H1-receptor antagonist, e.g., loratadine. For example, a metered dose inhaler (e.g., for 120 actuations) was prepared containing cilomilast 18 mg, loratadine 12 mg, and 1,1,1,2-tetrafluoroethane to 75.0 mg.

IT 257892-33-4

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comps. comprising PDE-4 inhibitor and H1-receptor antagonist for treatment of respiratory diseases)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:965129 CAPLUS

DOCUMENT NUMBER: 138:44711

TITLE: Pharmaceutical compositions based on anticholinergics and PDE-IV inhibitors

INVENTOR(S): Pairret, Michel; Meade, Christopher J. M.; Pieper, Michael P.

PATENT ASSIGNEE(S): Germany

SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Provisional Ser. No. 281,857.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002193393	A1	20021219	US 2002-93240	20020307
DE 10110772	A1	20020912	DE 2001-10110772	20010307
US 2004024007	A1	20040205	US 2003-613783	20030703
US 2005148562	A1	20050707	US 2004-6940	20041208
PRIORITY APPLN. INFO.:			DE 2001-10110772	A 20010307
			US 2001-281857P	P 20010405

DE 2000-10054042	A	20001031
US 2000-253613P	P	20001128
DE 2000-10062712	A	20001215
DE 2000-10063957	A	20001220
US 2000-257220P	P	20001221
US 2000-257221P	P	20001221
DE 2001-10111058	A	20010308
DE 2001-10113366	A	20010320
US 2001-281653P	P	20010405
US 2001-281874P	P	20010405
DE 2001-10138272	A	20010810
US 2001-314599P	P	20010824
US 2001-7182	B1	20011019
US 2001-86145	B1	20011019
US 2001-27662	B1	20011220
DE 2002-10206505	A	20020216
US 2002-92116	A1	20020306
US 2002-93240	B1	20020307
US 2002-100659	A1	20020318
US 2002-369213P	P	20020401
US 2003-360064	A2	20030207
US 2003-413065	B2	20030414
US 2003-419358	A1	20030421
US 2003-613783	A2	20030703
US 2004-763894	A2	20040123
US 2004-775901	A2	20040210
US 2004-776757	A2	20040211
US 2004-824391	A2	20040414

OTHER SOURCE(S): MARPAT 138:44711

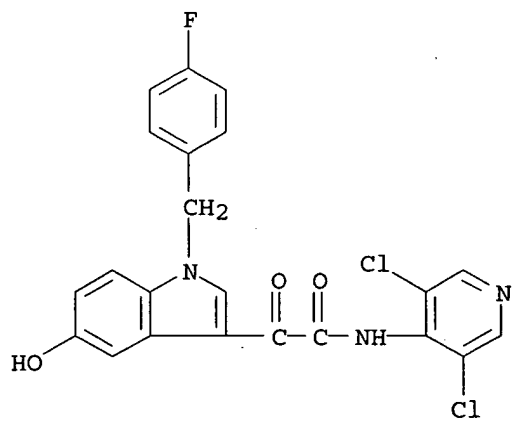
AB The present invention relates to novel pharmaceutical compns. based on anticholinergics and phosphodiesterase (PDE) IV inhibitors, processes for preparing them and their use in the treatment of respiratory tract diseases. For example, a suspension aerosol contained tiotropium bromide 0.029%, AWD 12-281 0.033%, ethanol 0.5%, iso-Pr myristate 0.1%, and TG 227 to 100%.

IT 257892-33-4, AWD 12-281

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalation compns. based on anticholinergics and phosphodiesterase IV inhibitors for treatment of respiratory tract diseases)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:695761 CAPLUS
 DOCUMENT NUMBER: 137:237718
 TITLE: Inhalant compositions containing anticholinergics and
 PDE IV inhibitors
 INVENTOR(S): Meade, Christopher John Montague; Pairet, Michel;
 Pieper, Michael Paul
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
 SOURCE: PCT Int. Appl., 34 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 14
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069945	A2	20020912	WO 2002-EP1988	20020226
WO 2002069945	A3	20030130		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10110772	A1	20020912	DE 2001-10110772	20010307
CA 2439763	AA	20020912	CA 2002-2439763	20020226
EP 1372649	A2	20040102	EP 2002-727329	20020226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004521134	T2	20040715	JP 2002-569122	20020226
BR 2002007883	A	20040727	BR 2002-7883	20020226
NZ 528621	A	20050429	NZ 2002-528621	20020226
CN 1649588	A	20050803	CN 2002-805346	20020226
ZA 2003006221	A	20040722	ZA 2003-6221	20030812
PRIORITY APPLN. INFO.:			DE 2001-10110772	A 20010307
			WO 2002-EP1988	W 20020226

OTHER SOURCE(S): MARPAT 137:237718

AB The invention relates to drug compns. based on anticholinergics and PDE IV inhibitors, to methods for their production, and to their use as inhalants for the treatment of respiratory tract diseases. Thus an inhalation powder was composed of capsules that contained (µg/capsule): tiotropium bromide 21.7; AWD-12-281 200; lactose 4778.3.

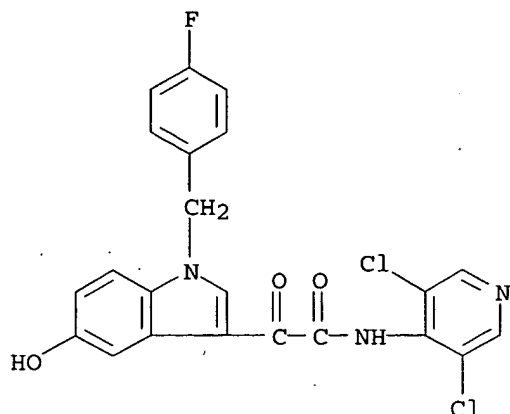
IT 257892-33-4, AWD-12-281

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(inhalant compns. containing anticholinergics and PDE IV inhibitors)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy-α-oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:575737 CAPLUS

DOCUMENT NUMBER: 137:135500

TITLE: Methods of inducing ovulation by administering a non-polypeptide cAMP level modulator

INVENTOR(S): Palmer, Stephen; McKenna, Sean; Tepper, Mark; Eshkol, Aliza; MacNamee, Michael C.

PATENT ASSIGNEE(S): Applied Research Systems Holding N.V., USA

SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U.S. Ser. No. 928,268.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002103106	A1	20020801	US 2001-14812	20011214
US 6953774	B2	20051011		
US 2002065324	A1	20020530	US 2001-928268	20010810
CA 2469939	AA	20030626	CA 2001-2469939	20011214
AU 2002217111	A1	20030630	AU 2002-217111	20011214
EP 1463493	A1	20041006	EP 2001-274987	20011214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001017198	A	20041026	BR 2001-17198	20011214
CN 1582146	A	20050216	CN 2001-823951	20011214
JP 2005516924	T2	20050609	JP 2003-552277	20011214
US 2005148501	A1	20050707	US 2003-498639	20011214
US 2006003925	A1	20060105	US 2005-169183	20050628
PRIORITY APPLN. INFO.:			US 2000-224962P	P 20000811
			US 2001-928268	A2 20010810
			US 2001-14812	A3 20011214
			WO 2001-EP14730	W 20011214

AB The present invention relates to methods of inducing ovulation in a female host comprising the administration of a non-polypeptide cAMP level modulator to the female host. In another aspect, the invention provides for specific administration of the phosphodiesterase inhibitor prior to the luteal phase of the host's ovulatory cycle. Preferred non-polypeptide cAMP level modulator include phosphodiesterase inhibitors, particularly

inhibitors of phosphodiesterase 4 isoforms. Pharmaceutical compns. containing the cAMP modulators are also claimed.

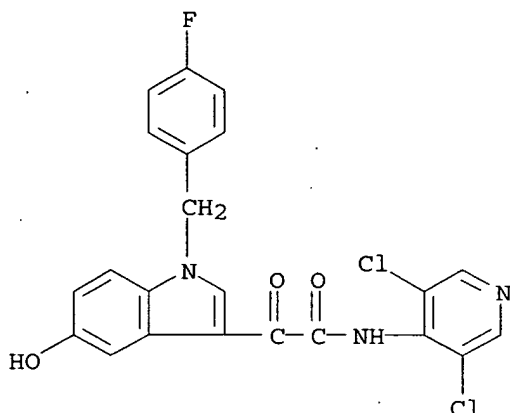
IT 257892-33-4, AWD-12-281

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods of inducing ovulation by administering a non-polypeptide cAMP level modulator)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 31 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:495906 CAPLUS

DOCUMENT NUMBER: 138:117605

TITLE: Effects of the phosphodiesterase 4 inhibitors SB 207499 and AWD 12-281 on the inflammatory reaction in a model of allergic dermatitis

AUTHOR(S): Baumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim; Ehinger, Andreas M.; Ehinger, Britt; Kietzmann, Manfred

CORPORATE SOURCE: Toxicology and Pharmacy, Department of Pharmacology, School of Veterinary Medicine, Hanover, 30559, Germany

SOURCE: European Journal of Pharmacology (2002), 446(1-3), 195-200

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The inhibitors of the phosphodiesterase 4, SB 207499 (cilomilast, c-4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)-r-L-cyclohexane carboxylic acid) and AWD 12-281 (N-(3,5-dichloropyrid-4-yl)-[1-(4-fluorobenzyl)-5-hydroxyindole-3-yl]glyoxylic acid amide) were tested in a model of allergic dermatitis in mice. To obtain an allergic dermatitis, BALB/c mice were sensitized to toluene-2,4-diisocyanate. The allergic reaction was challenged by topical administration of toluene-2,4-diisocyanate onto the mice ears. Before challenge, two groups of mice were treated topically (ear skin) with SB 207499 or AWD 12-281. There was a significant ear swelling in toluene-2,4-diisocyanate-challenged mice ears 4, 8, 16, 24 and 48 h after challenge. SB 207499 and AWD 12-281 inhibited this swelling significantly 8, 16, 24 and 48 h after the challenge. For

biochem. parameters and histol., ears were sampled from mice sacrificed 4, 8 and 16 h after the challenge. In homogenized tissue, SB 207499 and AWD 12-281 inhibited significantly the secretion of interleukin 1 β induced by toluene-2,4-diisocyanate 4 and 8 h after challenge. The cell influx (granulocytes) observed in the toluene-2,4-diisocyanate-challenged mice 8 and 16 h after challenge was nearly abolished by AWD 12-281 and SB 204799.

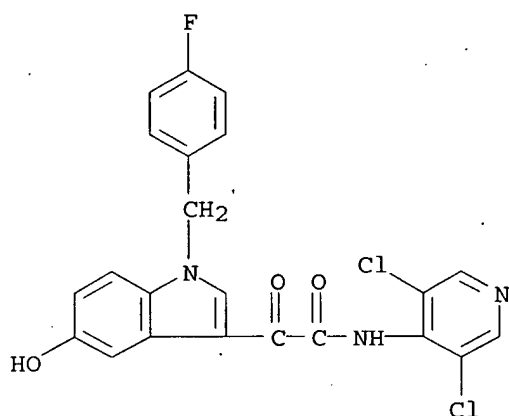
IT 257892-33-4, AWD 12-281

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effects of phosphodiesterase 4 inhibitors SB 207499 and AWD 12-281 on inflammatory reaction in a model of allergic dermatitis)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:850920 CAPLUS

DOCUMENT NUMBER: 135:366766

TITLE: Method for enhancing cognitive function with phosphodiesterase-4 inhibitors

INVENTOR(S): Hagan, James

PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK

SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

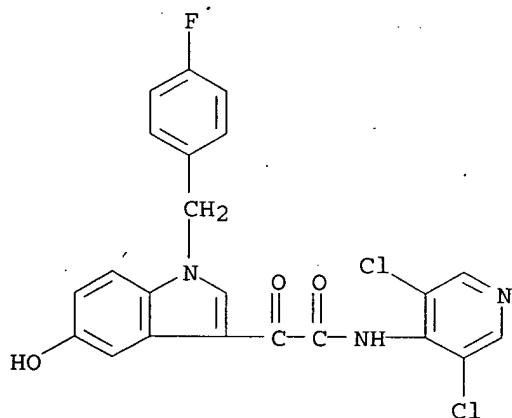
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087281	A2	20011122	WO 2001-GB2134	20010515
WO 2001087281	A3	20020328		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
 UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 EP 1292287 A2 20030319 EP 2001-929824 20010515
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP. 2003533473 T2 20031111 JP 2001-583749 20010515
 US 2003187006 A1 20031002 US 2003-275853 20030314
 PRIORITY APPLN. INFO.: GB 2000-11802 A 20000516
 WO 2001-GB2134 W 20010515
 AB. A method for enhancing cognitive function by administering to a patient in
 need thereof an effective amount of a PDE4 inhibitor.
 IT 257892-33-4, AWD-12-281
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (enhancing cognitive function with phosphodiesterase-4 inhibitors)
 RN 257892-33-4 CAPLUS
 CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-
 fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 33 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2001:380415 CAPLUS
 DOCUMENT NUMBER: 134:361385
 TITLE: Combined phosphodiesterase 3 (PDE3) and
 phosphodiesterase 4 (PDE4) inhibitor therapy for the
 treatment of obesity
 INVENTOR(S): Snyder, Peter
 PATENT ASSIGNEE(S): Icos Corporation, USA
 SOURCE: PCT Int. Appl., 30 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----

WO 2001035979 A2 20010525 WO 2000-US42137 20001113
 WO 2001035979 A3 20020103

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165418P P 19991113

AB Materials and methods are provided for the treatment of obesity that involve a combination of a PDE3 and PDE4 inhibitor in synergistically effective amts. Methods for producing PDE proteins are also described.

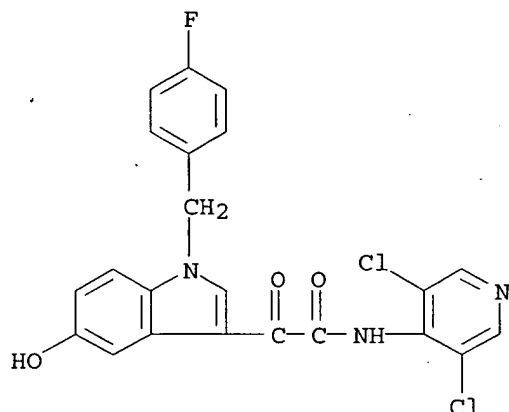
IT 257892-33-4, AWD-12-281

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phosphodiesterase 3 and phosphodiesterase 4 inhibitor combination therapy for treatment of obesity)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



L25 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:260010 CAPLUS

DOCUMENT NUMBER: 135:86768

TITLE: Requirement of additional adenylate cyclase activation for the inhibition of human eosinophil degranulation by phosphodiesterase IV inhibitors

AUTHOR(S): Ezeamuzie, C. I.

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Faculty of Medicine, P.O. Box 24923, Kuwait University, Safat, 13110, Kuwait

SOURCE: European Journal of Pharmacology (2001), 417(1/2), 11-18

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human eosinophils contain predominantly phosphodiesterase type IV, but selective inhibitors of this isoenzyme fail to inhibit certain eosinophil responses such as degranulation. In this study, the effect of activation of adenylate cyclase on the ability of several highly selective PDE IV inhibitors to inhibit complement C5a-induced O2- release and degranulation of human eosinophils in vitro was investigated. All four selective PDE IV inhibitors, N-(3,5-dichloropyrid-4-yl)-3-cyclopentyl-oxy-4-methoxybenzamide (RP 73401), rolipram, N-(3,5-dichloropyrid-4-yl)-[1-(4-fluorobenzyl)-5-hydroxy-indol-3-yl]glyoxylacidamide (AWD 12-281) and c-4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl-r-1-cyclohexane carboxylic acid) (SB 207499) potently inhibited C5a-induced O2- generation (IC50=0.03, 0.42, 0.55 and 0.86 μ M, resp.), but generally failed to inhibit degranulation. The only exception was AWD 12-281, which inhibited degranulation (IC50=16.2 μ M). In the presence of different AC activators (histamine, salbutamol, prostaglandin E2 and forskolin), the PDE IV inhibitors became potent inhibitors of degranulation. The interaction between the PDE IV inhibitors and the AC activators resulted in a synergistic increase in intracellular levels of adenosine 3', 5'-monophosphate (cAMP). These results show that PDE IV inhibitors generally require an addnl. cAMP signal to be able to inhibit eosinophil degranulation, and that this signal can be generated via both membrane receptors and direct AC activation. This may be relevant to the in vivo effectiveness of PDE IV inhibitors in eosinophilic inflammation.

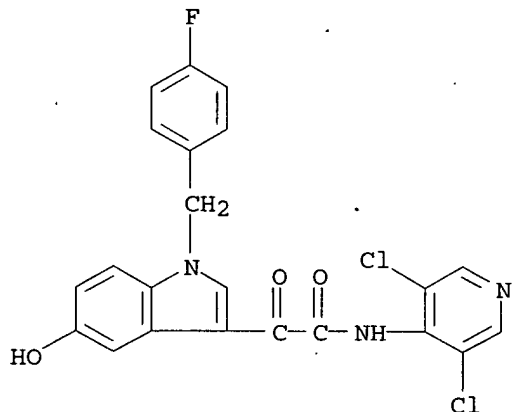
IT 257892-33-4, AWD 12-281

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(requirement of addnl. adenylate cyclase activation for inhibition of human eosinophil degranulation by phosphodiesterase IV inhibitors)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:259980 CAPLUS

DOCUMENT NUMBER: 135:57779

TITLE: Identification of inhibitor binding sites of the cAMP-specific phosphodiesterase 4

AUTHOR(S): Richter, W.; Unciuleac, L.; Hermsdorf, T.; Kronbach, T.; Dettmer, D.
 CORPORATE SOURCE: Medical Faculty, Institute of Biochemistry, University of Leipzig, Leipzig, D-04103, Germany
 SOURCE: Cellular Signalling (2001), 13(4), 287-297
 CODEN: CESIEY; ISSN: 0898-6568
 PUBLISHER: Elsevier Science Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

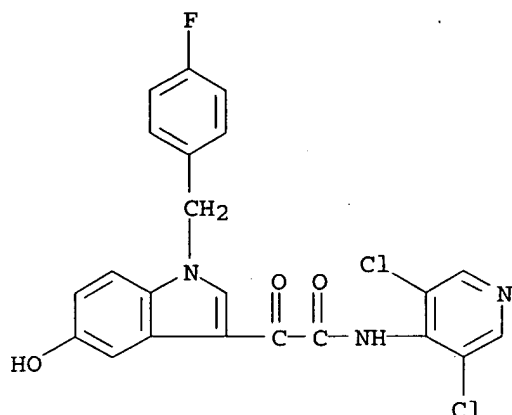
AB Using the technique of site-directed mutagenesis, point mutants of human PDE4A have been developed in order to identify amino acids involved in inhibitor binding. Relevant amino acids were selected according to a peptidic binding site model for PDE4 inhibitors, which suggests interaction with two tryptophan residues, one histidine and one tyrosine residue, as well as one Zn²⁺ ion. Mutations were directed at those tryptophan, histidine, and tyrosine residues, which are conserved among the PDE4 subtypes (PDE4A-D) and lie within the high-affinity 4-[3-(cyclopentoxyl)-4-methoxyphenyl]-2-pyrrolidone (rolipram) binding domain of human PDE4A (amino acids 276-681 according to the PDE4A sequence L20965). Truncations to this region do not alter enzyme activity or inhibitor sensitivity. The mutants were expressed in COS1 cells, and the recombinant cyclic nucleotide phosphodiesterase (PDE) forms have been characterized in terms of their catalytic activity and inhibitor sensitivities. Tyrosine residues 432 and 602, as well as histidine 588, were found to be involved in inhibitor binding, but no interaction was detected between tryptophan and PDE inhibitors tested. To test the possibility that other amino acids are of importance for hydrophobic interactions, selected phenylalanine residues were also mutated. We found phenylalanine 613 and 645 to influence inhibitor binding to PDE4. The significant differences in the inhibitor sensitivities of the mutants show that the various inhibitors have different enzyme binding sites. Based on the assumption that the known side effects of PDE4 inhibitors (like emesis and nausea) are caused directly by selective inhibition of different conformation states of PDE4, our results may be a hint to differ between PDE4 inhibitors, which have emetic side effects (like rolipram), and those that do not have side effects (like N-(3,5-dichloropyrid-4-yl)-[1-(4-fluorbenzyl)-5-hydroxy-indol-3-yl]-glyoxylateamide [AWD12-281]) by the differences of their binding sites and in that context contribute to the development of novel drugs. Furthermore, the identification of amino acid interactions proposed by the peptidic binding site model, which was used for the mutant selection, verifies the PrGen modeling as a useful method for the prediction of inhibitor binding sites in cases where detailed knowledge of the protein structure is not available.

IT 257892-33-4, AWD12-281

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (identification of inhibitor binding sites of cAMP-specific phosphodiesterase 4)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:30560 CAPLUS

DOCUMENT NUMBER: 134:221365

TITLE: The effect of selective and non-selective phosphodiesterase inhibitors on allergen- and leukotriene C4-induced contractions in passively sensitized human airways

AUTHOR(S): Schmidt, Dunja T.; Watson, Nikki; Dent, Gordon; Ruhlmann, Elke; Branscheid, Detlev; Magnussen, Helgo; Rabe, Klaus F.

CORPORATE SOURCE: Department of Pulmonology, Leiden University Medical Centre, Leiden, NL-2333 ZA, Neth.

SOURCE: British Journal of Pharmacology (2000), 131(8), 1607-1618

CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Non-selective inhibitors of cyclic nucleotide phosphodiesterase (PDE) block allergen-induced contraction of passively sensitized human airways in vitro by a dual mechanism involving a direct relaxant effect on smooth muscle and inhibition of histamine and cysteinyl leukotriene (LT) release from airways. We investigated the effects of non-selective PDE inhibitors and selective inhibitors of PDE3 and PDE4 in order to determine the involvement of PDE isoenzymes in the suppression of allergic bronchoconstriction. Macroscopically normal airways from 76 patients were sensitized with IgE-rich sera (>250 u ml⁻¹) containing specific antibodies against allergen (*Dermatophagoides farinae*). Contractile responses of bronchial rings were assessed using standard organ bath techniques. Passive sensitization caused increased contractile responses to allergen, histamine and LTC₄. Non-selective PDE inhibitors (theophylline, 3-isobutyl-1-methylxanthine [IBMX]), a PDE3-selective inhibitor (motapizone), PDE4-selective inhibitors (RP73401, rolipram, AWD 12-281) and a mixed PDE3/4 inhibitor (zardaverine) all significantly relaxed inherent bronchial tone at resting tension and to a similar degree. Theophylline, IBMX, zardaverine and the combination of motapizone and RP73401 inhibited the contractile responses to allergen and LTC₄. Pre-treatment with motapizone, RP73401, rolipram or the methylxanthine adenosine receptor antagonist, 8-phenyltheophylline, did not significantly decrease responses to either allergen or LTC₄. We

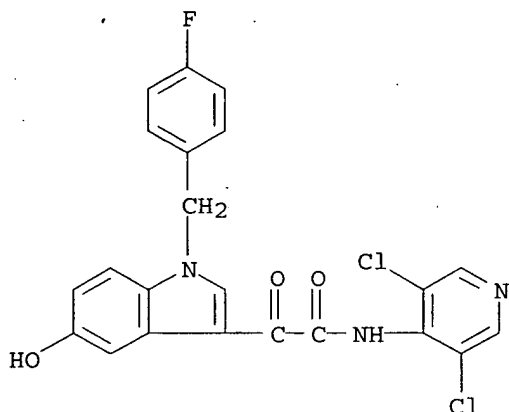
conclude that combined inhibition of PDE3 and PDE4, but not selective inhibition of either isoenzyme or antagonism of adenosine receptors, is effective in suppressing allergen-induced contractions of passively sensitized human airways. The relationship between allergen- and LTC4-induced responses suggests that PDE inhibitors with PDE3 and PDE4 selectivity are likely to act in part through inhibition of mediator release and not simply through direct relaxant actions on airway smooth muscle.

IT 257892-33-4, AWD 12-281

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(phosphodiesterase inhibitors in allergen- and leukotriene C4-induced contractions in sensitized human airways)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:647583 CAPLUS

DOCUMENT NUMBER: 132:145941

TITLE: Therapeutic potential of phosphodiesterase 4 inhibitors in allergic diseases

AUTHOR(S): Crocker, I. Caroline; Townley, Robert G.

CORPORATE SOURCE: Creighton University Allergic Disease Center, Omaha, NE, USA

SOURCE: Drugs of Today (1999), 35(7), 519-535

CODEN: MDACAP; ISSN: 0025-7656

PUBLISHER: Prous Science

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 137 refs. CAMP is thought to be associated with inflammatory cell activity: high levels tend to decrease proliferation and cytokine secretion, whereas low concns. have the opposite effect (1). Since many phosphodiesterases (PDEs) degrade cAMP, inhibitors of this enzyme decrease inflammatory cell activity. Theophylline, which has nonselective PDE inhibitor activity in addition to its other mechanisms of action, has been used in the treatment of asthma for many years. Unfortunately, because of the important role of PDEs in the cell, nonspecific inhibition of these

enzymes causes many undesirable side effects. The discovery of PDE isoenzyme families (PDE1-PDE10), their subtypes (HPDE4 and LPDE4) and their differential distribution among the cell types, as well as their specific functions in controlling cell processes, has led to the development of new, specific PDE4 inhibitors. This review details the rationale for the use of PDE4 inhibitors in the treatment of allergic disease. In addition, the effects of PDE4 inhibitors in vitro, in preclin. animal models and in the clinic are covered. Finally, up-to-date information on the most recently developed inhibitors, such as SB-207499, CDP-840, AWD-12-281 and D-4418, is provided.

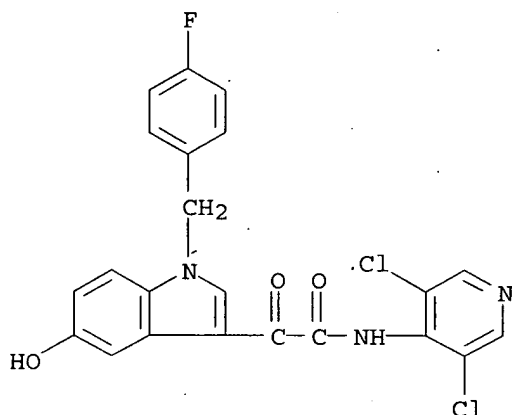
IT 257892-33-4, AWD 12-281

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic potential of phosphodiesterase 4 inhibitors in allergic diseases)

RN 257892-33-4 CAPLUS

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 137 THERE ARE 137 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:175908 CAPLUS

DOCUMENT NUMBER: 128:217285

TITLE: Preparation of new, N-substituted indole-3-glyoxylamides as antiasthmatics, antiallergic agents and immunosuppressants/immunomodulators

INVENTOR(S): Lebaut, Guillaume; Menciu, Cecilia; Kutscher, Bernhard; Emig, Peter; Szelenyi, Stefan; Brune, Kay

PATENT ASSIGNEE(S): Asta Medica Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

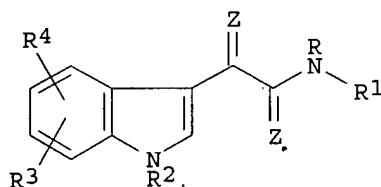
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
------------	------	------	-----------------	------

 WO 9809946 A1 19980312 WO 1997-EP4474 19970816
 W: AU, BR, CN, CZ, EE, HU, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RU,
 SG, SK, TR, UA
 RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
 DE 19636150 A1 19980312 DE 1996-19636150 19960906
 AU 9740158 A1 19980326 AU 1997-40158 19970816
 AU 726521 B2 20001109
 EP 931063 A1 19990728 EP 1997-937586 19970816
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI
 CN 1227542 A 19990901 CN 1997-197128 19970816
 BR 9712808 A 19991123 BR 1997-12808 19970816
 JP 2000505098 T2 20000425 JP 1998-512167 19970816
 JP 3296437 B2 20020702
 NZ 334476 A 20000526 NZ 1997-334476 19970816
 IL 127798 A1 20030731 IL 1997-127798 19970816
 CN 1496980 A 20040519 CN 2002-2002132061 19970816
 RU 2237661 C2 20041010 RU 1999-106782 19970816
 ZA 9707475 A 19980219 ZA 1997-7475 19970820
 CA 2215013 AA 19980306 CA 1997-2215013 19970904
 CA 2215013 C 20020305
 US 6008231 A 19991228 US 1997-925326 19970908
 TW 550256 B 20030901 TW 1997-86112985 19970930
 NO 9901071 A 19990304 NO 1999-1071 19990304
 NO 314725 B1 20030512
 US 6344467 B1 20020205 US 1999-409263 19990930
 US 2002161025 A1 20021031 US 2002-58836 20020130
 NO 2003000481 A 19990304 NO 2003-481 20030130
 US 2003207892 A1 20031106 US 2003-402931 20030401
 US 6919344 B2 20050719

PRIORITY APPLN. INFO.:

DE 1996-19636150 A 19960906
 WO 1997-EP4474 W 19970816
 US 1997-925326 A3 19970908
 US 1999-409263 A3 19990930
 US 2002-58836 B1 20020130

OTHER SOURCE(S): MARPAT 128:217285
 GI



I

AB The title compds. [I; R = H, (un)substituted C1-6 alkyl; R1 = (un)substituted Ph, pyridyl, pyrimidinyl, etc.; RR1 = atoms to close (N-substituted) piperazine ring; R2 = H, (un)substituted C1-6 alkyl, (un)substituted benzoyl; R3, R4 = H, OH, C1-6 alkyl, C3-7 cycloalkyl, halo, NO2, amino, benzyloxy, etc.; Z = O, S] and their acid salts were prepared, e.g., by N-alkylation of indoles with R2-bearing reactants followed by acylation with a dicarbonyl halide and amidation of the remaining acid halide function. For example, a title compound I (R = R3 = R4 = H, R1 = 4-pyridyl, R2 = 4-FC6H4CH2, Z = O) (preparation by benzylation of

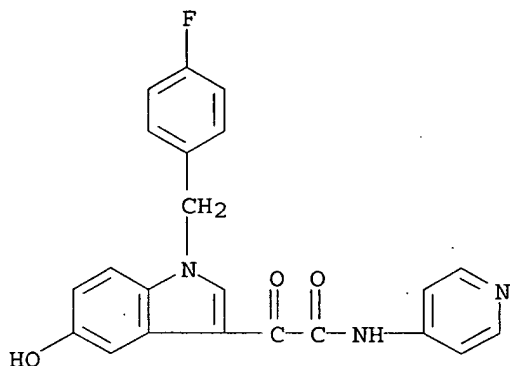
indole with 4-FC₆H₄CH₂Cl, acylation of the intermediate with (COCl)₂ and amidation of the acyl chloride with 4-aminopyridine given) at 10 mg/kg i.p. in guinea pigs gave 55.4% inhibition of allergen-induced late-phase eosinophilia, vs. 47.0 for cyclosporin A.

IT 204206-02-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-substituted indoleglyoxylamides as antiasthmatics, antiallergic agents and immunosuppressants/immunomodulators)

RN 204206-02-0 CAPLUS

CN 1H-Indole-3-acetamide, 1-[(4-fluorophenyl)methyl]-5-hydroxy- α -oxo-N-4-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:571228 CAPLUS

DOCUMENT NUMBER: 117:171228

TITLE: Preparation of N-(azabicycloalkyl)indole-3-glyoxylamides and analogs as 5-HT antagonists

INVENTOR(S): Clark, Robin D.; Eglen, Richard M.; Muchowski, Joseph M.; Smith, William L.; Weinhardt, Klaus K.

PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA

SOURCE: Eur. Pat. Appl., 38 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

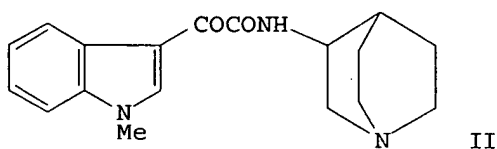
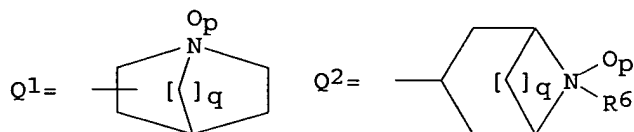
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 490263	A1	19920617	EP 1991-120856	19911204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
<u>US 5192770</u>	A	19930309	US 1990-624028	19901207
FI 9105736	A	19920608	FI 1991-5736	19911205
CA 2057181	AA	19920608	CA 1991-2057181	19911206
NO 9104825	A	19920609	NO 1991-4825	19911206
AU 9188856	A1	19920611	AU 1991-88856	19911206
AU 644249	B2	19931202		
HU 60270	A2	19920828	HU 1991-3836	19911206

JP 04290884	A2	19921015	JP 1991-322979	19911206
ZA 9109660	A	19930607	ZA 1991-9660	19911206
PRIORITY APPLN. INFO.:			US 1990-624028	A 19901207
OTHER SOURCE(S):	MARPAT 117:171228			
GI				



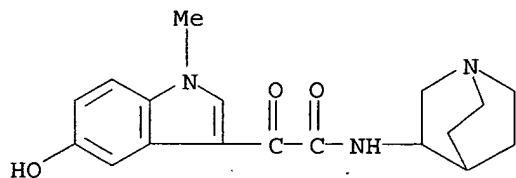
AB R1COCONR2R3 [I; R1 = (substituted) Ph, -indolo, -2-oxobenzimidazolo, -3-benzofuranyl, -3-indolyl, etc.; R2 = azabicycloalkyl groups Q1, Q2, etc.; R3 = H, alkyl; R6 = alkyl; p = 0, 1; q = 1-3] were prepared. Thus, 1-methyl- α -oxo-3-indoleacetyl chloride was condensed with (S)-3-amino-1-azabicyclo[2.2.2]octane to give title compound (S)-II which reversed atropine-induced cognitive deficit in mice at .apprx.1 mg/kg orally.

IT 143137-41-1P 143137-42-2P 143137-43-3P
143339-42-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as 5-HT antagonist)

RN 143137-41-1 CAPLUS

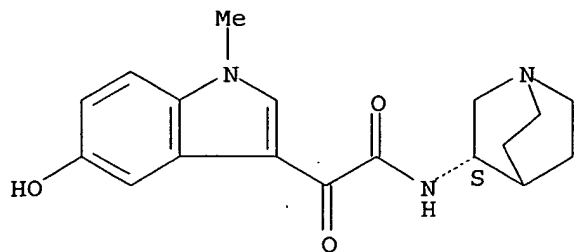
CN 1H-Indole-3-acetamide, N-1-azabicyclo[2.2.2]oct-3-yl-5-hydroxy-1-methyl- α -oxo- (9CI) (CA INDEX NAME)



RN 143137-42-2 CAPLUS

CN 1H-Indole-3-acetamide, N-1-azabicyclo[2.2.2]oct-3-yl-5-hydroxy-1-methyl- α -oxo-, (S)- (9CI) (CA INDEX NAME)

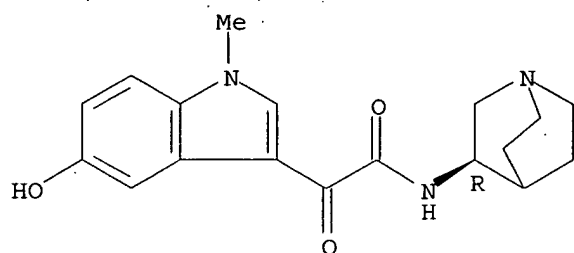
Absolute stereochemistry.



RN 143137-43-3 CAPLUS

CN 1H-Indole-3-acetamide, N-1-azabicyclo[2.2.2]oct-3-yl-5-hydroxy-1-methyl- α -oxo-, (R)- (9CI) (CA INDEX NAME)

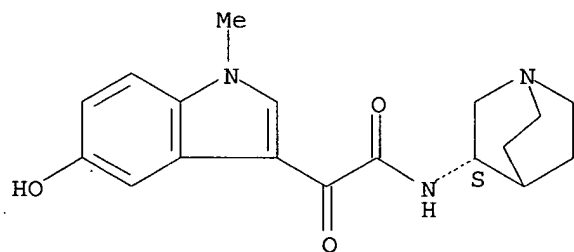
Absolute stereochemistry.



RN 143339-42-8 CAPLUS

CN 1H-Indole-3-acetamide, N-1-azabicyclo[2.2.2]oct-3-yl-5-hydroxy-1-methyl- α -oxo-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L25 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1969:413112 CAPLUS

DOCUMENT NUMBER: 71:13112

TITLE: Recent progress in rifamycin derivatives chemistry

AUTHOR(S): Maggi, Nicola; Sensi, Piero

CORPORATE SOURCE: Res. Lab., Lepetit S.p.A., Milan, Italy

SOURCE: Int. Congr. Chemother., Proc., 5th (1967), Volume 1, Issue 1, 15-21. Editor(s): Spitzzy, K. H. Verlag Wien. Med. Akad.: Vienna, Austria.

CODEN: 20JJA4

DOCUMENT TYPE:

Conference

LANGUAGE:

English

GI For diagram(s), see printed CA Issue.

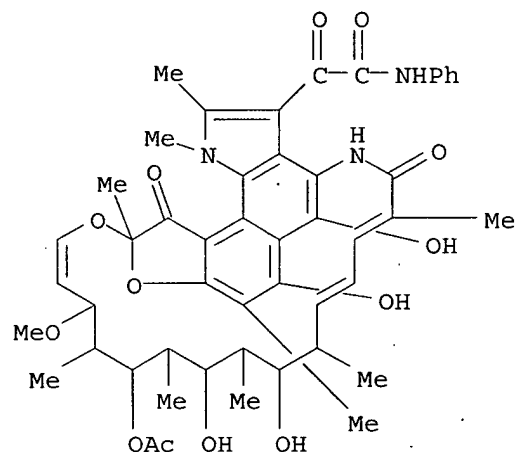
AB Cf. CA 65: 12597c. An investigation of derivs. of 3-formylrifamycin SV (I) bearing amino groups on the side chain is reported. O-substituted oximes, N-substituted imines and hydrazones of I are cited. None is as active on *Staphylococcus aureus* as Rifampicin. A new series of rifamycins with a pyrrole nucleus condensed in positions 3 and 4 is also reported. These products are obtained by reaction of rifamycin S with allyl amines. The structure of the resulting 3,4-pyrrolorifamycins (II) was confirmed by N.M.R. and uv. Bacterial activity is dependent upon size of substituents R, R₁, and R₂. In the presence of Et₃N the same reaction yields products with a hydroquinone structure (III). The N.M.R. spectrum shows the presence of a methinic hydrogen.

IT 22912-69-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 22912-69-2 CAPLUS

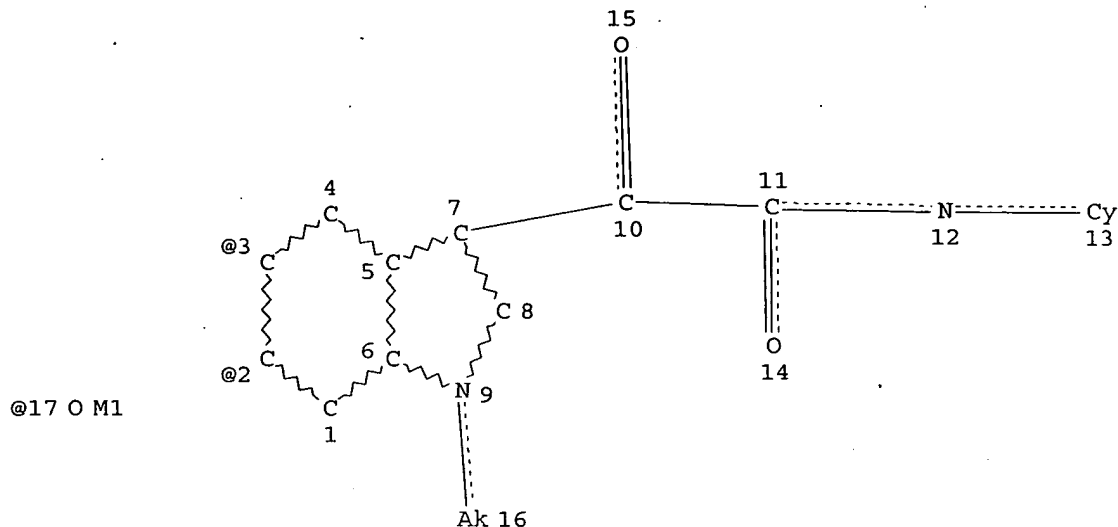
CN 9,4-(Epoxy-pentadeca[1,11,13]trienimino)-1H-benzofuro[5,4-g]indole-3-glyoxylanilide, 9,10-dihydro-5,6,16,18,20-pentahydroxy-14-methoxy-1,2,7,9,15,17,19,21,25-nonamethyl-10,26-dioxo-, 16-acetate (8CI) (CA INDEX NAME)



=> d que 124

```
L1 ( 74)SEA FILE=CAPLUS ABB=ON PLU=ON ("RUNDFELDT C"/AU OR "RUNDFELDT
CHRIS"/AU)
L2 ( 51)SEA FILE=CAPLUS ABB=ON PLU=ON ("KUSS H"/AU OR "KUSS H H"/AU
OR "KUSS H J"/AU OR "KUSS H M"/AU OR "KUSS HILDEGARD"/AU)
L3 ( 12)SEA FILE=CAPLUS ABB=ON PLU=ON ("HOFGEN N"/AU OR "HOFGEN
NORBERT"/AU)
L4 9 SEA FILE=CAPLUS ABB=ON PLU=ON (L1 AND (L2 OR L3)) OR (L2 AND
L3)
L5 ( 74)SEA FILE=CAPLUS ABB=ON PLU=ON ("RUNDFELDT C"/AU OR "RUNDFELDT
CHRIS"/AU)
L6 ( 51)SEA FILE=CAPLUS ABB=ON PLU=ON ("KUSS H"/AU OR "KUSS H H"/AU
OR "KUSS H J"/AU OR "KUSS H M"/AU OR "KUSS HILDEGARD"/AU)
L7 ( 12)SEA FILE=CAPLUS ABB=ON PLU=ON ("HOFGEN N"/AU OR "HOFGEN
```

NORBERT"/AU)
 L8 126 SEA FILE=CAPLUS ABB=ON PLU=ON (L5 OR L6 OR L7)
 L16 STR



VPA 17-2/3 U

NODE ATTRIBUTES:

HCOUNT	IS M1	AT 17
NSPEC	IS R	AT 1
NSPEC	IS R	AT 2
NSPEC	IS R	AT 3
NSPEC	IS R	AT 4
NSPEC	IS R	AT 5
NSPEC	IS R	AT 6
NSPEC	IS R	AT 7
NSPEC	IS R	AT 8
NSPEC	IS R	AT 9
NSPEC	IS C	AT 10
NSPEC	IS C	AT 11
NSPEC	IS C	AT 12
NSPEC	IS C	AT 13
NSPEC	IS C	AT 14
NSPEC	IS C	AT 15
NSPEC	IS C	AT 16
NSPEC	IS C	AT 17

DEFAULT MLEVEL IS ATOM

MLEVEL IS CLASS AT 10 11 12 14 15 16 17

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE

L19	35 SEA FILE=REGISTRY SSS FUL L16
L20	51 SEA FILE=CAPLUS ABB=ON PLU=ON L19
L22	11 SEA FILE=CAPLUS ABB=ON PLU=ON L20 AND L8
L24	14 SEA FILE=CAPLUS ABB=ON PLU=ON (L4 OR L22)

=> d ibib abs 124 tot

L24 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:226501 CAPLUS

DOCUMENT NUMBER: 144:267237

TITLE: The phosphodiesterase 4 inhibitor AWD 12-281 is active in a new guinea-pig model of allergic skin inflammation predictive of human skin penetration and suppresses both Th1 and Th2 cytokines in mice

AUTHOR(S): Hoppmann, Joachim; Baeumer, Wolfgang; Galetzka, Christin; Hoefgen, Norbert; Kietzmann, Manfred; Rundfeldt, Chris

CORPORATE SOURCE: Department of Pharmacology, elbion AG, Radebeul, D-01445, Germany

SOURCE: Journal of Pharmacy and Pharmacology (2005), 57(12), 1609-1617

CODEN: JPPMAB; ISSN: 0022-3573

PUBLISHER: Pharmaceutical Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The selective phosphodiesterase 4 (PDE4) inhibitor AWD 12-281 is structurally optimized for topical administration. It has potent effects in models of lung inflammation if administered as a dry powder inhalation. It has also demonstrated its anti-inflammatory property in a mouse model of cutaneous inflammation after topical administration. The aim of this study was to evaluate whether AWD 12-281 may be capable of penetrating human skin. Therefore a new guinea-pig model of allergic skin inflammation had to be developed. In ovalbumin-sensitized guinea-pigs, intracutaneous administration of ovalbumin results in a rapid development of allergic skin wheals. Topically administered AWD 12-281 was capable of reducing the development of wheals, indicating that this compound can penetrate the stratum corneum of guinea-pig skin as a predictor of human skin penetration. A secondary aim was the evaluation of a T cell subtype preference of AWD 12-281 since PDE4 inhibitors are said to preferentially inhibit Th2-type cytokines. Therefore, the effects of AWD 12-281 on a broad spectrum of Th1- and Th2-type cytokines were studied in tissue homogenates after allergen challenge in sensitized mice and in supernatants of anti CD3/anti-CD28-stimulated peripheral blood mononuclear cells (PBMCs). In both models, AWD 12-281 suppressed both T cell subtype cytokines indicating a broad spectrum activity of AWD 12-281. A further issue was to determine the duration of action and the concentration-response relation of the topical activity of AWD 12-281 using a model of acute local inflammation - the arachidonic-acid-induced mouse ear edema. The compound exhibited a dose-dependent effect with a minimally effective concentration of 0.3%; after repeated administration the minimally effective concentration was 0.03%. A single administration of a 3% solution resulted in significant suppression of inflammation even 48 h after treatment. In conclusion, our results indicate that AWD 12-281 is a very promising drug candidate not only for the treatment of lung inflammation using inhalative administration but also for the treatment of atopic dermatitis.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

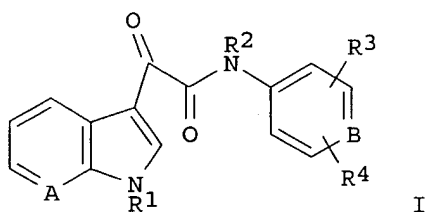
ACCESSION NUMBER: 2004:927204 CAPLUS

DOCUMENT NUMBER: 141:395538

TITLE: Preparation of 7-azaindolyglyoxylamides as phosphodiesterase IV inhibitors.

INVENTOR(S): Hoefgen, Norbert; Kuss, Hildegard; Olbrich,
 Matthias; Egerland, Ute; Rundfeldt, Chris;
 Steinike, Karin; Schindler, Rudolf
 PATENT ASSIGNEE(S): Elbion A.-G., Germany
 SOURCE: PCT Int. Appl., 58 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094416	A1	20041104	WO 2004-EP4339	20040423
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10318610	A1	20041111	DE 2003-10318610	20030424
US 2004224971	A1	20041111	US 2004-826136	20040416
AU 2004232483	A1	20041104	AU 2004-232483	20040423
CA 2523063	AA	20041104	CA 2004-2523063	20040423
EP 1613627	A1	20060111	EP 2004-729102	20040423
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR			
PRIORITY APPLN. INFO.:			DE 2003-10318610	A 20030424
			WO 2004-EP4339	W 20040423
OTHER SOURCE(S):	MARPAT 141:395538			
GI				

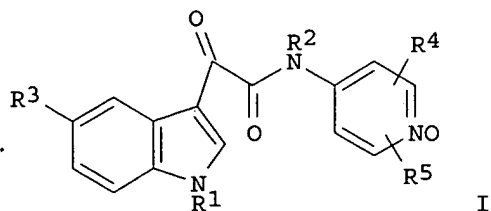


AB Title compds. [I; A = N, N-oxide group; B = C, N, N-oxide group; R1 = (substituted) alkyl, alkenyl; R2 = H, alkyl; R3, R4 = H, alkyl, OH, SH, NH2, NO2, cyano, SO3H, CO2H, alkoxycarbonyl, halo, alkoxy, alkylthio, (substituted) Ph, pyridyl, etc.], were prepared Thus, N-(3,5-dichloropyridin-4-yl) [1-(4-fluorobenzyl)-7-azaindol-3-yl]glyoxylic acid amide in CH2Cl2 was treated dropwise with m-chloroperbenzoic acid in HOAc followed by stirring for 7 days to give 9.4% N-(3,5-dichloropyridin-4-yl) [1-(4-fluorobenzyl)-7-oxo-7-azaindol-3-yl]glyoxylic acid amide. I inhibited phosphodiesterase 4 with IC50's in the range of 10-10 M to 10-5 M.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:927194 CAPLUS
 DOCUMENT NUMBER: 141:395426
 TITLE: Preparation of N-oxopyridinyl hydroxyindolylglyoxylamides as phosphodiesterase IV inhibitors.
 INVENTOR(S): Hoefgen, Norbert; Kuss, Hildegard; Steinike, Karin; Egerland, Ute; Rundfeldt, Chris; Pfeifer, Thomas
 PATENT ASSIGNEE(S): Elbion A.-G., Germany
 SOURCE: PCT Int. Appl., 41 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094406	A1	20041104	WO 2004-EP4340	20040423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10318609	A1	20041111	DE 2003-10318609	20030424
US 2004266760	A1	20041230	US 2004-824342	20040414
AU 2004232484	A1	20041104	AU 2004-232484	20040423
CA 2523062	AA	20041104	CA 2004-2523062	20040423
EP 1615911	A1	20060118	EP 2004-729060	20040423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004009683	A	20060418	BR 2004-9683	20040423
PRIORITY APPLN. INFO.:			DE 2003-10318609	A 20030424
			WO 2004-EP4340	A 20040423
OTHER SOURCE(S):		MARPAT 141:395426		
GI				



AB Title compds. [I; R1 = (substituted) alkyl, alkenyl; R2 = H, alkyl; R3 = OH; R4, R5 = H, alkyl, OH, SH, NH2, NO2, cyano, SO3H, CO2H, alkoxy, carbonyl, halo, alkoxy, alkylthio, (substituted) Ph, pyridyl, etc.], were prepared. Thus, N-(3,5-dichloropyridin-4-yl) [5-benzyloxy-1-(4-fluorobenzyl)indol-3-yl]glyoxylamide in CH2Cl2 was treated dropwise with m-chloroperbenzoic acid in HOAc followed by stirring for 7 days to give 16.1% pyridine N-oxide derivative, which was refluxed with BBr3 in CH2Cl2 to give 72.8% N-(3,5-dichloro-1-oxopyridin-4-yl) [1-(4-fluorobenzyl)-5-hydroxyindol-3-yl]glyoxylamide. I inhibited phosphodiesterase 4 with IC50's in the range of 10⁻⁵ M to 10⁻¹⁰ M.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:927193 CAPLUS

DOCUMENT NUMBER: 141:395425

TITLE: Preparation of hydroxyindolylglyoxylic acid oxopyridinylamides as phosphodiesterase IV inhibitors.

INVENTOR(S): Hoefgen, Norbert; Kuss, Hildegard; Steinike, Karin; Egerland, Ute; Rundfeldt, Chris

PATENT ASSIGNEE(S): Elbion A.-G., Germany

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

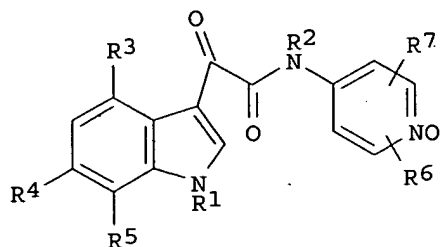
DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094405	A1	20041104	WO 2004-EP4338	20040423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10318611	A1	20041111	DE 2003-10318611	20030424
US 2004242643	A1	20041202	US 2004-825862	20040416
AU 2004232482	A1	20041104	AU 2004-232482	20040423
CA 2523048	AA	20041104	CA 2004-2523048	20040423
EP 1615912	A1	20060118	EP 2004-729109	20040423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
PRIORITY APPLN. INFO.:			DE 2003-10318611	A 20030424
			WO 2004-EP4338	W 20040423
OTHER SOURCE(S):		MARPAT 141:395425		
GI				



AB Title compds. [I; R1 = (substituted) alkyl, alkenyl; R2 = H, alkyl; R3-R5 = H, OH; ≥ 1 or R3-R5 = OH; R6, R7 = H, alkyl, OH, SH, NH₂, NO₂, cyano, SO₃H, CO₂H, alkylcarbonyloxy, halo, alkylthio, (substituted) Ph, pyridyl, etc.], were prepared. Thus, N-(3,5-dichloropyridin-4-yl) [7-benzyloxy-1-(4-fluorobenzyl)indol-3-yl]glyoxylic acid amide was stirred 7 days with m-chloroperbenzoic acid in HOAc to give 16.9% pyridine N-oxide derivative, which was refluxed with BBr₃ in CH₂Cl₂ to give 66.2% N-(3,5-dichloro-1-oxopyridin-4-yl) [1-(4-fluorobenzyl)-7-hydroxyindol-3-yl]glyoxylic acid amide. I inhibited phosphodiesterase 4 with IC₅₀'s in the range of 10⁻¹⁰ M to 10⁻⁵ M.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:450478 CAPLUS

DOCUMENT NUMBER: 141:23423

TITLE: Preparation of 4- and/or 7-hydroxyindoles as phosphodiesterase 4 inhibitors

INVENTOR(S): Hoefgen, Norbert; Kuss, Hildegard; Egerland, Ute; Rundfeldt, Chris; Hartenhauer, Helge; Gasparic, Antje

PATENT ASSIGNEE(S): Elbion Ag, Germany

SOURCE: Ger. Offen., 17 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

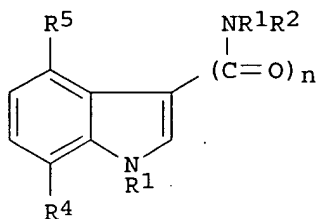
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10253426	A1	20040603	DE 2002-10253426	20021115
DE 10253426	B4	20050922		
US 2004147759	A1	20040729	US 2003-714568	20031113
CA 2505988	AA	20040603	CA 2003-2505988	20031114
WO 2004045607	A1	20040603	WO 2003-EP12742	20031114
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003283400	A1	20040615	AU 2003-283400	20031114

EP 1562584 A1 20050817 EP 2003-775355 20031114
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 BR 2003016234 A 20051011 BR 2003-16234 20031114
 JP 2006508141 T2 20060309 JP 2004-552596 20031114
 NO 2005002864 A 20050613 NO 2005-2864 20050613
 PRIORITY APPLN. INFO.: DE 2002-10253426 A 20021115
 WO 2003-EP12742 W 20031114
 OTHER SOURCE(S): MARPAT 141:23423
 GI



AB Title compds. [I; n = 1, 2; R1 = (substituted) (branched) alkyl, (substituted) (branched) unsatd. alkenyl; R2, R3 = H, (substituted) alkyl, pyridyl, etc.; R4, R5 = H, OH], were prepared. Thus, a suspension of NaH in THF was dropwise treated with 4-amino-3,5-dichloropyridine in THF followed by stirring for 1 h at 20°. The reaction mixture was dropwise treated with 7-benzyloxy-1-(4-chlorobenzyl)-indol-3-ylglyoxyloyl chloride (preparation given) at 0° followed by reflux for 4 h to give 47.5% N-(3,5-dichloropyridin-4-yl)-[1-(4-chlorobenzyl)-7-hydroxyindol-3-yl]glyoxyamide. The latter inhibited phosphodiesterase 4 (PDE 4) with IC50 = 0.002 µmol/L.

L24 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:216863 CAPLUS
 DOCUMENT NUMBER: 140:247052
 TITLE: Treatment nonallergic rhinitis by selective phosphodiesterase 4 inhibitors
 INVENTOR(S): Rundfeldt, Chris; Kuss, Hildegard;
 Hofgen, Norbert
 PATENT ASSIGNEE(S): Elbion A.-G., Germany
 SOURCE: Ger. Offen., 12 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10241407	A1	20040318	DE 2002-10241407	20020906
US 2004116501	A1	20040617	US 2003-654365	20030903
CA 2497374	AA	20040318	CA 2003-2497374	20030905
WO 2004022041	A2	20040318	WO 2003-EP9895	20030905
WO 2004022041	A3	20040506		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
 PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2003271586 A1 20040329 AU 2003-271586 20030905
 EP 1534272 A2 20050601 EP 2003-753390 20030905
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 BR 2003014031 A 20050705 BR 2003-14031 20030905
 CN 1678307 A 20051005 CN 2003-821089 20030905
 JP 2005539058 T2 20051222 JP 2004-533499 20030905
 ZA 2005001582 A 20050909 ZA 2005-1582 20050222
 NO 2005001468 A 20050603 NO 2005-1468 20050321
 PRIORITY APPLN. INFO.: DE 2002-10241407 A 20020906
 WO 2003-EP9895 W 20030905

OTHER SOURCE(S): MARPAT 140:247052

AB The invention discloses the use of hydroxyindolylglyoxylic acid amides as inhibitors of the phosphodiesterase 4 for the treatment of nonallergic rhinitis.

L24 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:130977 CAPLUS

DOCUMENT NUMBER: 140:281023

TITLE: Anti-inflammatory potential of the selective phosphodiesterase 4 inhibitor N-(3,5-dichloro-pyrid-4-yl)-[1-(4-fluorobenzyl)-5-hydroxy-indole-3-yl]-glyoxylic acid amide (AWD 12-281), in human cell preparations

AUTHOR(S): Draheim, Regina; Egerland, Ute; **Rundfeldt, Chris**

CORPORATE SOURCE: Departments of Pharmacology and Molecular Biology, Elbion AG, Radebeul, Germany

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 308(2), 555-563

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB AWD 12-281 is a potent (IC₅₀ = 9.7 nM) and highly selective inhibitor of the phosphodiesterase 4 (PDE4) isoenzyme with low affinity to the high-affinity rolipram-binding site. The compound was optimized for topical treatment of asthma, chronic obstructive pulmonary disease (COPD), and allergic rhinitis. The aim of the present study was to assess the effect of AWD 12-281 in human inflammatory cells. Peripheral blood mononuclear cells (PBMCs), diluted whole blood, and human nasal polyp cells derived from surgically resected nasal polyps from patients with polyposis comprise sources of target tissue cells that can be used to predict anti-inflammatory effects in patients. AWD 12-281 was capable of suppressing the production of cytokines in stimulated PBMCs: interleukin-2 (IL-2, phytohemagglutinin stimulation), IL-5 (Con A stimulation), IL-5 and IL-4 (anti-CD3/anti-CD28 co-stimulation), and lipopolysaccharide-stimulated release of tumor necrosis factor α (TNF α). The corresponding values for half-maximum inhibition, EC₅₀, for AWD 12-281 were within a narrow range (46-121 nM). Comparing the effect of AWD 12-281 with roflumilast, cilomilast (SB 207499), rolipram (RPR-73401), and

1-(3-nitrophenyl)-3-(4-pyridylmethyl)pyrido[2,3-d]pyrimidin-2,4(1H,3H)-dione (RS-25344-000), it could be shown that the PDE4 inhibitory activity was closely correlated with inhibitory potential as measured by the above-described assays. AWD 12-281 was also shown to suppress TNF α release in dispersed nasal polyps (EC50 = 111 nM) and in diluted whole blood (EC50 = 934 nM). The reduced activity in human blood may be related to high plasma protein binding. Currently, phase II clin. studies are under way to evaluate the therapeutic potential of AWD 12-281 in asthma, COPD, and allergic rhinitis.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:60309 CAPLUS

DOCUMENT NUMBER: 140:105273

TITLE: Topical treatment of skin diseases

INVENTOR(S): Rundfeldt, Chris; Kietzmann, Manfred; Hoppmann, Joachim; Baeumer, Wolfgang; Kuss, Hildegard; Hoefgen, Norbert

PATENT ASSIGNEE(S): Elbion AG, Germany

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006920	A1	20040122	WO 2003-EP7514	20030710
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004038958	A1	20040226	US 2003-611649	20030701
CA 2492093	AA	20040122	CA 2003-2492093	20030710
AU 2003254332	A1	20040202	AU 2003-254332	20030710
BR 2003012696	A	20050426	BR 2003-12696	20030710
EP 1531818	A1	20050525	EP 2003-763810	20030710
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2005537262	T2	20051208	JP 2004-520586	20030710
ZA 2005000108	A	20050223	ZA 2005-108	20050106
NO 2005000718	A	20050401	NO 2005-718	20050210
PRIORITY APPLN. INFO.:			US 2002-395221P	P 20020711
			WO 2003-EP7514	W 20030710

OTHER SOURCE(S): MARPAT 140:105273

AB The present invention relates to a method for the treatment of an inflammatory and/or allergic skin disease comprising topically administering a substituted hydroxy indole which is a phosphodiesterase 4 inhibitor. Examples are provided of the topical effectiveness of AWD 12-281 and cilomilast in dermal immunol. inflammation.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:2852 CAPLUS

DOCUMENT NUMBER: 140:59520

TITLE: Preparation of pyrrolidine and piperidinecarboxamides as inhibitors of phosphodiesterase IV (PDE 4)

INVENTOR(S): Egerland, Ute; Rueger, Carla; Schindler, Rudolf; Rundfeldt, Chris; Kuss, Hildegard; Lichoscherstow, Arkadi M.; Seredenin, Sergey B.; Borissenko, Sergey A.

PATENT ASSIGNEE(S): Elbion A.-G., Germany

SOURCE: PCT Int. Appl., 79 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

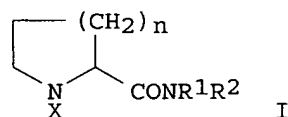
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000806	A1	20031231	WO 2003-EP6590	20030623
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10228132	A1	20040122	DE 2002-10228132	20020624
AU 2003245979	A1	20040106	AU 2003-245979	20030623
PRIORITY APPLN. INFO.:			DE 2002-10228132	A 20020624
			WO 2003-EP6590	W 20030623

OTHER SOURCE(S): MARPAT 140:59520

GI



AB Title compds. [I; n = 1, 2; X = NH₂, N:CR₃R₄; NHCHR₃R₄; NR₃CHR₃R₄; NHCH₂R₄, NHCOR₄; R₁, R₄ = (substituted) 3-14 membered (saturated) (poly)cyclyl; 5-15 membered (saturated) (poly)heterocyclyl; R₂ = H, (substituted) (branched) alkyl, PhCH₂; NR₁R₂ = (substituted) heterocyclyl, R₃ = H, (substituted) (branched) alkyl], were prepared Thus, 1-amino-pyrrolidine-2-carboxylic acid, 2,6-dichlorophenylamide, and 3,4-dimethoxybenzaldehyde in 2-propanol were refluxed for 4 h to give 84% N-(2,6-dichlorophenyl)-(E)-1-([(3,4-dimethoxyphenyl)methylene]amino)pyrrolidine-2-carboxamide. Several I at 114-5,000 nmol/L inhibited PDE 4 with IC₅₀ = 32.4-79.6%.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:775804 CAPLUS

DOCUMENT NUMBER: 140:104940

TITLE: In vivo efficacy in airway disease models of
N-(3,5-dichloropyrid-4-yl)-[1-(4-fluorobenzyl)-5-
hydroxyindole-3-yl]glyoxylic acid amide (AWD 12-281),
a selective phosphodiesterase 4 inhibitor for inhaled
administration

AUTHOR(S): Kuss, H.; Hoefgen, N.; Johanssen, S.;
Kronbach, T.; Rundfeldt, C.

CORPORATE SOURCE: Department of Pharmacology, Elbion AG, Radebeul,
Germany

SOURCE: Journal of Pharmacology and Experimental Therapeutics
(2003), 307(1), 373-385

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental
Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB AWD 12-281 is a highly potent and selective phosphodiesterase 4 (PDE4) inhibitor that was designed to have a metabolic profile that was optimized for topical administration. The aim of the current study was to explore the pharmacol. profile of intratracheally administered AWD 12-281 in different models of asthma and chronic obstructive pulmonary disease (COPD) in comparison with steroids. To assess the anti-inflammatory potential of AWD 12-281, the antigen-induced cell infiltration in bronchoalveolar lavage fluid (BALF) of Brown Norway rats was determined AWD 12-281 (ID50 of 7 µg/kg i.t.) as well as beclomethasone (0.1 µg/kg i.t.) suppresses late-phase eosinophilia when administered intrapulmonary. Furthermore, AWD 12-281 has also strong anti-inflammatory properties when tested in lipopolysaccharide-induced acute lung neutrophilia in Lewis rats (ID50 of 0.02 µg/kg i.t.), ferrets (ID50 of 10 µg/kg i.t.), and domestic pigs (2-4 mg/pig i.t. or 1 mg/kg i.v.). In pigs, AWD 12-281 was as effective as beclomethasone (0.4 mg/pig i.t.) and dexamethasone (0.28 mg/kg i.v.), although at 3 to 10 times the dosage. The bronchodilatory activity of AWD 12-281 was assessed in sensitized guinea pigs. AWD 12-281 (1.5 mg/kg i.t., 1-h pretreatment) inhibited allergen-induced bronchoconstriction by 68% (parameter airway resistance). In sensitized BP-2 mice AWD 12-281 abolished the allergen-induced bronchial hyperresponsiveness and eosinophilia in BALF, showing dose dependence. When given orally, i.v. or i.t., AWD 12-281 has a considerably lower emetic potential than cilomilast in ferrets and roflumilast in pigs. When given topically by inhalation, no emesis could be induced in dogs up to the highest feasible dose (15 mg/kg in 50% lactose blend). These results indicate that AWD 12-281 is a unique potential new drug for the topical treatment of asthma and COPD.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:695438 CAPLUS

DOCUMENT NUMBER: 140:87294

TITLE: AWD 12-281, a highly selective phosphodiesterase 4
inhibitor, is effective in the prevention and
treatment of inflammatory reactions in a model of
allergic dermatitis

AUTHOR(S): Baeumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim;
Ehinger, Andreas M.; Rundfeldt, Chris;

CORPORATE SOURCE: Kietzmann, Manfred
Department of Pharmacology, Toxicology and Pharmacy,
School of Veterinary Medicine, Hannover, D-30559,
Germany

SOURCE: Journal of Pharmacy and Pharmacology (2003), 55(8),
1107-1114
CODEN: JPPMAB; ISSN: 0022-3573

PUBLISHER: Pharmaceutical Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB AWD 12-281 (N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide), a phosphodiesterase 4 inhibitor, which is optimized for topical administration, was tested in a model of allergic dermatitis in mice. To obtain an allergic dermatitis, BALB/c mice were sensitized to toluene-2,4-diisocyanate (TDI). The allergic reaction was challenged by topical administration of TDI onto the mice ears. AWD 12-281 was tested for its anti-inflammatory potential by oral, i.p. and topical administration. The phosphodiesterase 4 inhibitor, cilomilast (SB 207499), and/or the corticosteroid, diflorasone diacetate, were used as reference compds. Given orally and i.p. 2 h before as well as 5 and 24 h after TDI challenge, AWD 12-281 showed no, or only a transient inhibition of the allergen-induced ear swelling, whereas cilomilast significantly inhibited this ear swelling. Applied topically onto the ears before TDI challenge, AWD 12-281, cilomilast and diflorasone diacetate caused total inhibition of ear swelling 24 h after challenge, confirmed by a decrease of the pro-inflammatory cytokines interleukin-4, interleukin-6 and macrophage inhibitory protein-2. Administered topically after TDI challenge as therapeutic intervention, AWD 12-281 and diflorasone diacetate caused significant inhibition of ear swelling; cilomilast failed to do so. These results indicate that topically administered AWD 12-281 may be potent in the prevention and treatment of allergic/inflammatory skin diseases.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:420229 CAPLUS

DOCUMENT NUMBER: 138:18980

TITLE: AWD 12-281

AUTHOR(S): Kuss, H.; Hofgen, N.; Egerland, U.; Heer, S.; Marx, D.; Szelenyi, I.; Schupke, H.; Gasparic, A.; Olbrich, M.; Hempel, R.; Hartenhauer, H.; Krone, D.; Berthold, K.; Kronbach, T.; Rundfeldt, C.

CORPORATE SOURCE: Arzneimittelwerk Dresden GmbH, Radebeul, D-01445, Germany

SOURCE: Drugs of the Future (2002), 27(2), 111-116
CODEN: DRFUD4; ISSN: 0377-8282

PUBLISHER: Prous Science

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Airway diseases such as bronchial asthma and chronic obstructive pulmonary disease (COPD) are chronic inflammatory diseases whose prevalence is increasing. Current research concerned with developing effective treatments for these conditions have focused on the search for alternatives to the standard corticosteroid antiinflammatory therapy. Selective phosphodiesterase 4 (PDE4) inhibitors have received a considerable amount of attention due to their ability to suppress the functions of several cell types involved in allergic and inflammatory disorders. The selective PDE4 inhibitor AWD 12-281 is the result of a

pharmacophore-based synthesis program wherein the optimization process was supported by ligand-based drug design methods. AWD 12-281 was selected for further development for its high affinity and selectivity for the human PDE4 isoenzyme and due to its potent activity and excellent tolerability in models of allergic rhinitis, asthma and COPD, especially after topical treatment.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:55462 CAPLUS

DOCUMENT NUMBER: 132:202635

TITLE: A peptidic binding site model for PDE 4 inhibitors

AUTHOR(S): Polymeropoulos, Emmanuel E.; Hofgen, Norbert

CORPORATE SOURCE: Department of Chemical Research, Corporate R and D
ASTA Medica Group, Frankfurt, D-60314, Germany

SOURCE: Quantitative Structure-Activity Relationships (1999),
18(6), 543-547

CODEN: QSARDI; ISSN: 0931-8771

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The pseudoreceptor modeling program PrGen was used to construct a peptidic binding site model for phosphodiesterase 4 inhibitors. A training set of 21 diverse compds. (rolipram, nitraquazone and xanthine derivs., imidazo pyrido pyrazinones and 5-oxyindoles) was used to construct the binding site surrogate consisting of five amino acid residues, a Zn+2 cofactor and an envelope of charged virtual particles. The model was validated by predicting the free energies of binding ΔG_{pred0} of ten ligands (rolipram, imidazo pyrido pyrazinones and 5-oxyindoles). In seven cases the prediction was satisfactory. The rms deviation [4] in ΔG_0 is 0.16 and 1.82 kcal/mol-resulting in an uncertainty in IC_{50} (or K_i) of 1.32 and 22.81-for the training and the test set resp., while the corresponding maximal prediction errors in ΔG_{pred0} were 0.27 kcal/mol and 4.50 kcal/mol.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:708761 CAPLUS

DOCUMENT NUMBER: 131:310549

TITLE: New hydroxyindoles and their use as phosphodiesterase
4 and TNF α inhibitors

INVENTOR(S): Hofgen, Norbert; Egerland, Ute; Poppe,
Hildegard; Marx, Degenhard; Szelenyi, Stefan;
Kronbach, Thomas; Polymeropoulos, Emmanuel; Heer,
Sabine

PATENT ASSIGNEE(S): Arzneimittelwerk Dresden GmbH, Germany

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955696	A1	19991104	WO 1999-EP2792	19990424
W: AU, BG, BR, BY, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG,				

KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA,
 UZ, YU, ZA, AM, AZ, MD, TJ, TM
 RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE

DE 19818964	A1	19991104	DE 1998-19818964	19980428
DE 19917504	A1	20001019	DE 1999-19917504	19990417
AU 9938229	A1	19991116	AU 1999-38229	19990424
AU 748403	B2	20020606		
BR 9910029	A	20001226	BR 1999-10029	19990424
TR 200003130	T2	20010122	TR 2000-200003130	19990424
EP 1076657	A1	20010221	EP 1999-920779	19990424
EP 1076657	B1	20040804		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI

JP 2002513017	T2	20020508	JP 2000-545856	19990424
NZ 507406	A	20021126	NZ 1999-507406	19990424
RU 2217422	C2	20031127	RU 2000-129678	19990424
AT 272631	E	20040815	AT 1999-920779	19990424
EP 1475377	A1	20041110	EP 2004-18391	19990424

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY

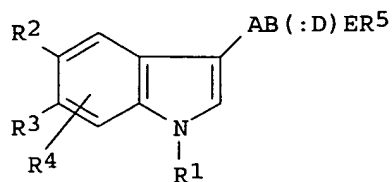
PT 1076657	T	20041130	PT 1999-920779	19990424
ES 2222706	T3	20050201	ES 1999-920779	19990424
CA 2270301	AA	19991028	CA 1999-2270301	19990428
US 6251923	B1	20010626	US 1999-300973	19990428
TW 530048	B	20030501	TW 1999-88106886	19990428
ZA 2000005540	A	20010327	ZA 2000-5540	20001010
BG 104842	A	20011031	BG 2000-104842	20001011
NO 2000005454	A	20001207	NO 2000-5454	20001027
HK 1035183	A1	20050415	HK 2001-105669	20010814
US 2002111351	A1	20020815	US 2002-80821	20020221
US 6545025	B2	20030408		
US 2002115651	A1	20020822	US 2002-81395	20020221
US 6545158	B2	20030408		
US 2002119971	A1	20020829	US 2002-81642	20020221
US 2002137745	A1	20020926	US 2002-81807	20020221
US 6602890	B2	20030805		
US 38624	E	20041012	US 2002-176435	20020919
US 2003134876	A1	20030717	US 2003-347659	20030120
US 6613794	B2	20030902		
US 2004220183	A1	20041104	US 2004-856034	20040527

PRIORITY APPLN. INFO.:

DE 1998-19818964	A	19980428
DE 1999-19917504	A	19990417
EP 1999-920779	A3	19990424
WO 1999-EP2792	W	19990424
US 1999-300973	A3	19990428
US 2000-653685	A3	20000901
US 2002-81642	A1	20020221
US 2002-81807	A3	20020221

OTHER SOURCE(S):
 GI

MARPAT 131:310549



I

AB Hydroxyindoles I [R1, R5 = (un)substituted aliphatic, carbocyclic, heterocyclic, spirocyclic; R2, R3 = H, OH, ≥ 1 of them being OH; R4 = H, (un)substituted OH, SH, S(O)H, SO₂H, NH₂, CO₂H, C(S)OH, NO₂, CN, F, Cl, Br, I; A = alkylene, alkenylene, (CHOZ)_m, CO, CS, C:NZ, O, S, NZ; Z = (un)substituted alkyl, alkenyl, carbocyclic, heterocyclic; B = C, S, SO; D = O, S, CH₂, NZ; E = bond, (CH₂)_m, O, S, NZ; m = 0-3] were prepared I have IC₅₀ for PDE IV inhibition of 1X10⁻⁹-1X10⁻⁵ and a selectivity relative to PDE's 2, 3, and 5 of 100-10,000. N-(3,5-dichloro-4-pyridyl)-2-[1-(4-fluorobenzyl)-5-methoxy-3-indolyl]-2-oxoacetamide was obtained by demethylation of the 5-methoxy compound and was reduced to the 2-hydroxyacetamide with NaBH₄.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Welcome to DIALOG

Dialog level 05.11.05D

Last logoff: 22may06 15:09:44

Logon file001 24may06 08:14:39

*** ANNOUNCEMENTS ***

NEW FILES RELEASED

***Regulatory Affairs Journals (File 183)

***Index Chemicus (File 302)

***Inspec (File 202)

RESUMED UPDATING

***File 141, Reader's Guide Abstracts

RELOADS COMPLETED

***File 516, D&B--Dun's Market Identifiers

***File 523, D&B European Dun's Market Identifiers

***File 531, American Business Directory

*** MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)

*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)

is now available online.

DATABASES REMOVED

***File 196, FINDEX

***File 468, Public Opinion Online (POLL)

Chemical Structure Searching now available in Prous Science Drug Data Report (F452), Prous Science Drugs of the Future (F453), IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus (File 302).

>>>For the latest news about Dialog products, services, content<<<

>>>and events, please visit What's New from Dialog at <<<

>>><http://www.dialog.com/whatsnew/>. You can find news about<<<

>>>a specific database by entering HELP NEWS <file number>.<<<

* * *

File 1:ERIC 1966-2006/Apr (c) format only 2006 Dialog

Set	Items	Description
-----	-------	-------------

---	-----	-----
-----	-------	-------

Cost is in DialUnits

?

Terminal set to DLINK

? b 5

24may06 08:14:45 User291213 Session D23.1

\$0.40 0.114 DialUnits File1

\$0.40 Estimated cost File1

\$0.02 TELNET

\$0.42 Estimated cost this search

\$0.42 Estimated total session cost 0.114 DialUnits

File 5:Biosis Previews(R) 1969-2006/May W2

(c) 2006 BIOSIS

Set	Items	Description
-----	-------	-------------

---	-----	-----
-----	-------	-------

? s nonallergic()rhinitis
 977 NONALLERGIC
 12748 RHINITIS
 S1 118 NONALLERGIC()RHINITIS
 ? s respira?
 S2 665326 RESPIRA?
 ? s s1 and s2
 118 S1
 665326 S2
 S3 62 S1 AND S2
 ? s s3 and py<=2002
 62 S3
 14134861 PY<=2002
 S4 46 S3 AND PY<=2002
 ? rd
 S5 46 RD (unique items)
 ? t s5/3,k/all

5/3,K/1

DIALOG(R)File 5:Biosis Previews(R)
 (c) 2006 BIOSIS. All rts. reserv.

0014007816 BIOSIS NO.: 200200601327

Preclinical evidence of azelastine hydrochloride activity

AUTHOR: Lieberman Phillip (Reprint)

AUTHOR ADDRESS: 300 Walnut Bend Road South, Cordova, TN, 38018, USA**USA

JOURNAL: Current Therapeutic Research 63 (9): p556-571 September, 2002
 2002

MEDIUM: print

ISSN: 0011-393X

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

2002

...ABSTRACT: literature published in the previous 15 years. The search terms used were azelastine, allergic rhinitis, **nonallergic rhinitis**, and anti-inflammatory activity. Results: In addition to having H1-blocking activity, azelastine has broad-based anti-inflammatory activity, probably accounting for its utility in the treatment of **nonallergic rhinitis**. The mechanisms governing its anti-inflammatory activity include prevention of mast cell and basophil degranulation...

DESCRIPTORS:

...MAJOR CONCEPTS: **Respiratory System**...

... **Respiration**

...DISEASES: immune system disease, **respiratory system disease**, drug therapy...

... **nonallergic rhinitis** --...

... **respiratory system disease**, drug therapy

5/3,K/2

DIALOG(R)File 5:Biosis Previews(R)
 (c) 2006 BIOSIS. All rts. reserv.

0013918696 BIOSIS NO.: 200200512207

Review of the upper airway, including olfaction, as mediator of symptoms
AUTHOR: Shusterman Dennis (Reprint)
AUTHOR ADDRESS: Upper Airway Biology Laboratory, University of California,
1301 S. 46th St., Bldg. 112, Richmond, CA, 94804, USA**USA
JOURNAL: Environmental Health Perspectives 110 (Supplement 4): p649-653
August, 2002 2002
MEDIUM: print
ISSN: 0091-6765
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

2002

...ABSTRACT: the chemical qualities of the air we breathe. A number of poorly understood conditions, including **nonallergic rhinitis**, irritant-induced rhinitis, odor-triggered asthma, odor-triggered panic attacks, chemical-induced olfactory dysfunction, and...

DESCRIPTORS:

...ORGANISMS: PARTS ETC: **respiratory** system
...DISEASES: **respiratory** system disease...

... **respiratory** system disease...

... **respiratory** system disease...

... **nonallergic rhinitis** --...

... **respiratory** system disease...

...immune system disease, **respiratory** system disease

5/3,K/3

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0013846124 BIOSIS NO.: 200200439635

Immunohistochemical localization of subtypes of muscarinic receptors in human inferior turbinate mucosa

AUTHOR: Nakaya Muneo (Reprint); Yuasa Takafumi; Usui Nobuo

AUTHOR ADDRESS: Dept of Otolaryngology, Tokyo University, Hongo 7-3-1, Bunkyo-Ku, 113-8655, Tokyo, Japan**Japan

JOURNAL: Annals of Otology Rhinology and Laryngology 111 (7): p593-597

July, 2002 2002

MEDIUM: print

ISSN: 0003-4894

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

2002

...ABSTRACT: the best target for more selective muscarinic drugs and guide the treatment of allergic and **nonallergic rhinitis**.

DESCRIPTORS:

MAJOR CONCEPTS: **Respiratory** System...

... **Respiration**

...ORGANISMS: PARTS ETC: **respiratory** system

5/3,K/4

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0013791230 BIOSIS NO.: 200200384741

Fluticasone propionate downregulates nasal fibroblast functions involved in airway inflammation and remodeling

AUTHOR: Silvestri M; Sabatini F; Scarso L; Cordone A; Dasic G; Rossi G A
(Reprint)

AUTHOR ADDRESS: Divisione di Pneumologia, Istituto G. Gaslini, Largo G. Gaslini, 5, I-16148, Genoa, Italy**Italy

JOURNAL: International Archives of Allergy and Immunology 128 (1): p51-58
May, 2002 2002

MEDIUM: print

ISSN: 1018-2438

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

2002

ABSTRACT: Background: Besides being highly effective in the treatment of allergic and **nonallergic rhinitis** with eosinophilia, intranasal corticosteroids appear to be useful in reducing nasal polypoid lesions and the...

DESCRIPTORS:

...ORGANISMS: PARTS ETC: **respiratory** system, inflammation, remodeling
...

... **respiratory** system, function, regulation

...DISEASES: immune system disease, **respiratory** system disease

5/3,K/5

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0013678385 BIOSIS NO.: 200200271896

Nasal lavage concentrations of free hemoglobin as a marker of microepistaxis during nasal provocation testing

AUTHOR: Park Y-J; Repka-Ramirez M S; Naranch K; Velarde A; Clauw D; Baraniuk J N (Reprint)

AUTHOR ADDRESS: Division of Rheumatology, Immunology and Allergy, Georgetown University, 3800 Reservoir Road, LL Gorman Building, Georgetown, USA**USA

JOURNAL: Allergy (Copenhagen) 57 (4): p329-335 April, 2002 2002

MEDIUM: print

ISSN: 0105-4538

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

2002

...ABSTRACT: saline nasal provocation. Unilateral hypertonic nasal provocation was performed in normal, allergic rhinitis (AR) and **nonallergic rhinitis** (NAR) subjects (total of 1316 specimens). fHb was measured using the Sigma-Aldrich kit (St...

...16.5 mug/ml. Elevations of fHb without changes in albumin were more

prevalent in **nonallergic rhinitis** . Conclusions: Significant bleeding into nasal lavage samples can contaminate the specimens and increase the concentrations...

DESCRIPTORS:

...DISEASES: immune system disease, **respiratory** system disease...

... **nonallergic rhinitis** --...

... **respiratory** system disease

CHEMICALS & BIOCHEMICALS: ...allergic rhinitis study, microepistaxis marker, nasal lavage fluid concentration, nasal provocation testing effects, **nonallergic rhinitis** study

5/3,K/6

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0013098525 BIOSIS NO.: 200100270364

Intranasal beclomethasone dipropionate in the treatment of common cold

AUTHOR: Qvarnberg Yrjo (Reprint); Valtonen Hannu; Laurikainen Kari

AUTHOR ADDRESS: Department of Otorhinolaryngology, Central Hospital of Central Finland, FIN-40620, Jyvaskyla, Finland**Finland

JOURNAL: Rhinology (Utrecht) 39 (1): p9-12 March, 2001 2001

MEDIUM: print

ISSN: 0300-0729

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

2001

ABSTRACT: Sinusitis is usually considered a complication of viral rhinitis. Virus infections in the upper **respiratory** tract lead to mucosal swelling, which may obstruct paranasal sinus outflow, resulting in infection in...

...been found beneficial in a variety of acute and chronic nasal conditions including allergic and **nonallergic rhinitis** and chronic rhinosinusitis. The purpose of this study was to examine whether the intranasal inhalation...

DESCRIPTORS:

...ORGANISMS: PARTS ETC: **respiratory** system...

...upper **respiratory** tract...

... **respiratory** system

...DISEASES: immune system disease, **respiratory** system disease...

... **respiratory** system disease, viral disease...

... **respiratory** system disease...

... **respiratory** system disease...

... **respiratory** system disease...

... **respiratory** system disease, viral disease

5/3,K/7

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0013002011 BIOSIS NO.: 200100173850

Expression of costimulatory CD80/CD86-CD28/CD152 molecules in nasal mucosa of patients with perennial allergic rhinitis

AUTHOR: Okano Mitsuhiro (Reprint); Hattori Hisashi (Reprint); Nagano Toshiaki; Takishita Teruaki (Reprint); Azuma Miyuki; Nishizaki Kazunori (Reprint)

AUTHOR ADDRESS: Okayama University Medical School, Okayama, Japan**Japan

JOURNAL: Journal of Allergy and Clinical Immunology 107 (2): pS150

February, 2001 2001

MEDIUM: print

CONFERENCE/MEETING: 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology New Orleans, Louisiana, USA March 16-21, 2001; 20010316

SPONSOR: American Academy of Allergy Asthma and Immunology

ISSN: 0091-6749

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

2001

DESCRIPTORS:

...ORGANISMS: PARTS ETC: **respiratory** system

...DISEASES: immune system disease, **respiratory** system disease, perennial...

... **nonallergic rhinitis** ---...

... **respiratory** system disease

5/3,K/8

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0012973402 BIOSIS NO.: 200100145241

Inflammatory cell and epithelial characteristics of perennial allergic and nonallergic rhinitis with a symptom history of 1 to 3 years' duration

AUTHOR: Amin Kawa (Reprint); Rinne Juhani; Haahtela Tari; Simola Markku; Peterson Christer G B; Roomans Godfried M; Malmberg Henrik; Venge Per; Seveus Lahja

AUTHOR ADDRESS: Department of Genetics and Pathology, Rudbecks Laboratory, University of Uppsala, SE-751 85, Uppsala, Sweden**Sweden

JOURNAL: Journal of Allergy and Clinical Immunology 107 (2 Part 2): p

249-257 February, 2001 2001

MEDIUM: print

ISSN: 0091-6749

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Inflammatory cell and epithelial characteristics of perennial allergic and nonallergic rhinitis with a symptom history of 1 to 3 years' duration
2001

...ABSTRACT: were obtained from 27 patients with perennial allergic rhinitis (PAR), from 12 patients with perennial **nonallergic rhinitis**

(PNAR) with eosinophils present in the nasal smear, and from 6 control subjects without rhinitis...

DESCRIPTORS:

...DISEASES: **respiratory** system disease, 1 to 3 year symptom history, allergic type, epithelial characteristics, inflammatory cell characteristics

5/3,K/9

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0012665654 BIOSIS NO.: 200000383967

Binding of glucocorticoids to human nasal tissue in vitro

AUTHOR: Esmailpour Nasser; Hoegger Petra; Rohdewald Peter (Reprint)

AUTHOR ADDRESS: Institute of Pharmaceutical Chemistry, Westfaelische Wilhelms-Universitaet, Hittorfstrasse 58-62, D-48149, Muenster, Germany** Germany

JOURNAL: International Archives of Allergy and Immunology 122 (2): p 151-154 June, 2000 2000

MEDIUM: print

ISSN: 1018-2438

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

2000

...ABSTRACT: Intranasal application of glucocorticoids is an efficacious treatment of allergic rhinitis and some cases of **nonallergic rhinitis**. However, no data on binding of glucocorticoids to nasal tissue are available. Pronounced binding of...

DESCRIPTORS:

...MAJOR CONCEPTS: **Respiratory** System...

... **Respiration**

...ORGANISMS: PARTS ETC: **respiratory** system...

... **respiratory** system disease

...DISEASES: immune system disease, **respiratory** system disease...

... **nonallergic rhinitis** --...

...immune system disease, **respiratory** system disease

5/3,K/10

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0012661216 BIOSIS NO.: 200000379529

Partial choanal atresia masking as allergic rhinitis

AUTHOR: Cox Ronald L (Reprint); Freeman Theodore M

AUTHOR ADDRESS: Department of Allergy and Immunology, Wilford Hall Medical Center, United States Air Force, 59th Medical Wing Lackland Air Force Base, San Antonio, TX, 78236, USA**USA

JOURNAL: Pediatric Asthma Allergy and Immunology 14 (2): p129-135 Summer, 2000 2000

MEDIUM: print

ISSN: 0883-1874

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

2000

...ABSTRACT: of approximately 30% of the population. Rhinitis can be classified into allergic rhinitis (AR) and **nonallergic rhinitis** (NAR). An interesting case of NAR is presented of a 4-year-old female with...

DESCRIPTORS:

...DISEASES: immune system disease, **respiratory** system disease...

...congenital disease, **respiratory** system disease

5/3,K/11

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0012624493 BIOSIS NO.: 200000342806

Immunolocalization of inducible nitric oxide synthase and 3-nitrotyrosine in the nasal mucosa of patients with rhinitis

AUTHOR: Kang Bor-Hwang; Chen Shinn-Shong; Jou Lin-Shu; Weng Pinh-Kun; Wang Hsing-Won (Reprint)

AUTHOR ADDRESS: Department of Otolaryngology, Tri-Service General Hospital, Ting-Chow Rd, 8 Section 3, Taipei, 100, Taiwan**Taiwan

JOURNAL: European Archives of Oto-Rhino-Laryngology 257 (5): p242-246 May, 2000 2000

MEDIUM: print

ISSN: 0937-4477

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

2000

...ABSTRACT: peroxyntirite in the pathogenesis of rhinitis. Inferior nasal turbinates were obtained from allergic rhinitis and **nonallergic rhinitis** patients during corrective nasal surgery. The expressions of the inducible form of nitric oxide synthase...

DESCRIPTORS:

...MAJOR CONCEPTS: **Respiratory** System...

... **Respiration**

...ORGANISMS: PARTS ETC: **respiratory** system

...DISEASES: **respiratory** system disease

5/3,K/12

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0012360297 BIOSIS NO.: 200000078610

Medical management of sinusitis

AUTHOR: Kaliner Michael (Reprint)

AUTHOR ADDRESS: Institute for Asthma and Allergy, Washington Hospital Center, Washington, DC, USA**USA

JOURNAL: American Journal of the Medical Sciences 316 (1): p21-28 July, 1998 1998

MEDIUM: print
ISSN: 0002-9629
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

1998

...ABSTRACT: abnormalities, and sinonasal microbiology. The most common events leading to sinusitis are colds, allergic and **nonallergic rhinitis**, and anatomic defects which interfere with the sinus outflow tracks. Treatment involves drainage of the...

DESCRIPTORS:

...ORGANISMS: PARTS ETC: **respiratory** system, drainage
...DISEASES: **respiratory** system disease, management

5/3,K/13

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0012217795 BIOSIS NO.: 199900477455

A controlled study on the effectiveness of loratadine in combination with flunisolide in the treatment of nonallergic rhinitis with eosinophilia (NARES)

AUTHOR: Purello-D'Ambrosio F (Reprint); Isola S; Ricciardi L; Gangemi S; Barresi L; Bagnato G F

AUTHOR ADDRESS: Istituto di Patologia Medica, Policlinico Universitario, Padiglione H, 98122, Messina, Italy**Italy

JOURNAL: Clinical and Experimental Allergy 29 (8): p1143-1147 Aug., 1999
1999

MEDIUM: print
ISSN: 0954-7894
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

...controlled study on the effectiveness of loratadine in combination with flunisolide in the treatment of nonallergic rhinitis with eosinophilia (NARES)

1999

ABSTRACT: Background **Nonallergic rhinitis** with eosinophilia (NARES), accounting for some 15% of perennial rhinitis, is a nasal disorder whose

...

DESCRIPTORS:

DISEASES: **nonallergic rhinitis** with eosinophilia...

...blood and lymphatic disease, **respiratory** system disease

5/3,K/14

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0012071140 BIOSIS NO.: 199900330800

Serum-soluble Fas levels as a marker to distinguish allergic and nonallergic rhinitis

AUTHOR: Kato Masashi (Reprint); Hattori Taku; Ito Hiroataka; Kageyama Motoo; Yamashita Tetsuji; Nitta Yukiko; Nakashima Izumi

AUTHOR ADDRESS: Department of Immunology, Nagoya University School of

Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya, Aichi, 466-8550, Japan**
Japan
JOURNAL: Journal of Allergy and Clinical Immunology 103 (6): p1213-1214
June, 1999 1999
MEDIUM: print
ISSN: 0091-6749
DOCUMENT TYPE: Article
RECORD TYPE: Citation
LANGUAGE: English

**Serum-soluble Fas levels as a marker to distinguish allergic and
nonallergic rhinitis
1999**

DESCRIPTORS:

...DISEASES: immune system disease, **respiratory** system disease...
... **nonallergic rhinitis** ----

... **respiratory** system disease

5/3,K/15

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0011895478 BIOSIS NO.: 199900155138

**ICAM-1 expression on sputum cells as a marker of persistent inflammation in
patients with allergic and nonallergic rhinitis and in asthmatics**

AUTHOR: Foresi A (Reprint); Leone C; Teodoro C; Mastropasqua B; Pelucchi A;
Chetta A; Fichera E; Burlone E; Olivieri D

AUTHOR ADDRESS: Serv. Fisopat. Respir., Sesto S. Giovanni, Parma, Italy**
Italy

JOURNAL: European Respiratory Journal 12 (SUPPL. 28): p370S Sept., 1998
1998

MEDIUM: print

CONFERENCE/MEETING: European Respiratory Society Annual Congress Geneva,
Switzerland September 19-23, 1998; 19980919

SPONSOR: The European Respiratory Society

ISSN: 0903-1936

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

**...expression on sputum cells as a marker of persistent inflammation in
patients with allergic and nonallergic rhinitis and in asthmatics
1998**

DESCRIPTORS:

...MAJOR CONCEPTS: **Respiratory** System...

... **Respiration**
...ORGANISMS: PARTS ETC: **respiratory** system
...DISEASES: immune system disease, **respiratory** system disease...

...immune system disease, **respiratory** system disease...

... **respiratory** system disease

5/3,K/16

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0011829707 BIOSIS NO.: 199900089367

Parameters for the diagnosis and management of sinusitis

AUTHOR: Joint Task Force On Practice Parameters

JOURNAL: Journal of Allergy and Clinical Immunology 102 (6 PART 2): p
1A-9A, S107-S144 Dec., 1998 1998

MEDIUM: print

ISSN: 0091-6749

DOCUMENT TYPE: Article; Standard

RECORD TYPE: Abstract

LANGUAGE: English

1998

...ABSTRACT: as "acute" when lasting 3 to 8 weeks and "chronic" when lasting longer. Viral upper **respiratory** infections frequently precede subsequent bacterial invasion of the sinuses by Streptococcus pneumoniae, Haemophilus influenzae, and...

...tests for immunodeficiency. Nasal cytology is useful in the clinical evaluation of underlying allergic rhinitis, **nonallergic rhinitis** with eosinophilia syndrome, nasal polyposis, and aspirin-sensitive patients. Quantitative sweat chloride tests for diagnosis...

DESCRIPTORS:

...DISEASES: **respiratory** system disease, diagnosis, practice parameters, management

5/3,K/17

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0011410854 BIOSIS NO.: 199800205101

Expression of histamine receptors in nasal epithelial cells and endothelial cells- the effects of sex hormones

AUTHOR: Hamano Nanako (Reprint); Terada Nobuhisa; Maesako Ken-Ichi; Ikeda Tatehiko; Fukuda Setsuya; Waita Jun; Yamashita Tetsuji; Konno Akiyoshi

AUTHOR ADDRESS: Dep. Otorhinolaryngology, Chiba Univ. Sch. Med., 1-8-1 Inohana, Chiba 260, Japan**Japan

JOURNAL: International Archives of Allergy and Immunology 115 (3): p
220-227 March, 1998 1998

MEDIUM: print

ISSN: 1018-2438

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

1998

...ABSTRACT: We compared the expressions on the specimens from patients with nasal allergy with those with **nonallergic rhinitis** or those from normal volunteers. In addition, we investigated the effects of female hormones on...

DESCRIPTORS:

...ORGANISMS: PARTS ETC: **respiratory** system...

... **respiratory** system

...DISEASES: immune system disease, **respiratory** system disease

5/3,K/18

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0011393523 BIOSIS NO.: 199800187770

Sense of smell in allergic and nonallergic rhinitis

AUTHOR: Simola M (Reprint); Malmberg H

AUTHOR ADDRESS: Helsinki Univ. Central Hosp., Dep. Otorhinolaryngol.,
Haartmaninkatu 4E, 00290 Helsinki, Finland**Finland

JOURNAL: Allergy (Copenhagen) 53 (2): p190-194 Feb., 1998 1998

MEDIUM: print

ISSN: 0105-4538

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Sense of smell in allergic and nonallergic rhinitis
1998

ABSTRACT: Hyposmia is a fairly common complaint in patients with
long-continuing allergic or **nonallergic rhinitis**. Other factors such
as aging, smoking, or nasal surgery may affect olfaction, but these have

...

DESCRIPTORS:

...DISEASES: **respiratory** system disease...

... **nonallergic rhinitis** --...

... **respiratory** system disease

5/3,K/19

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0011360200 BIOSIS NO.: 199800154447

**Quality of life of patients with allergic and nonallergic rhinitis : The
impact of allergy consultation and caregiver**

AUTHOR: Harvey R; Cvietusa P; Sanders B; Westley R; Marsh W; Williams J;
Conner D; Beck A; Speicher B

AUTHOR ADDRESS: Kaiser Permanente, Denver, CO, USA**USA

JOURNAL: Journal of Allergy and Clinical Immunology 101 (1 PART 2): pS180
Jan., 1998 1998

MEDIUM: print

CONFERENCE/MEETING: 54th Annual Meeting of the American Academy of Allergy,
Asthma and Immunology Washington, DC, USA March 13-18, 1998; 19980313

SPONSOR: American Academy of Allergy, Asthma, and Immunology

ISSN: 0091-6749

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

**Quality of life of patients with allergic and nonallergic rhinitis : The
impact of allergy consultation and caregiver**
1998

DESCRIPTORS:

...DISEASES: **respiratory** system disease, caregiver impact, treatment,
consultation impact...

... **respiratory** system disease, caregiver impact, consultation impact

5/3,K/20

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0011359929 BIOSIS NO.: 199800154176

Nasal lavage and capillary suction obtain different compartments of the nasal mucociliary system

AUTHOR: Ostertag P; Rasp G; Kramer M

AUTHOR ADDRESS: ENT Univ., Munich, Germany**Germany

JOURNAL: Journal of Allergy and Clinical Immunology 101 (1 PART 2): pS113
Jan., 1998 1998

MEDIUM: print

CONFERENCE/MEETING: 54th Annual Meeting of the American Academy of Allergy, Asthma and Immunology Washington, DC, USA March 13-18, 1998; 19980313

SPONSOR: American Academy of Allergy, Asthma, and Immunology

ISSN: 0091-6749

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

1998

DESCRIPTORS:

...ORGANISMS: PARTS ETC: **respiratory** system

...DISEASES: immune system disease, **respiratory** system disease...

... **nonallergic rhinitis** --...

...immune system disease, **respiratory** system disease

5/3,K/21

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0011321051 BIOSIS NO.: 199800115298

Comparison of nasal mucosal responsiveness to neuronal stimulation in non-allergic and allergic rhinitis: Effects of capsaicin nasal challenge

AUTHOR: Sanico A M; Philip G; Proud D; Naclerio R M; Togias A (Reprint)

AUTHOR ADDRESS: Johns Hopkins Asthma Allergy Cent., Unit Office 7, 5501
Hopkins Bayview Circle, Baltimore, MD 21224-6801, USA**USA

JOURNAL: Clinical and Experimental Allergy 28 (1): p92-100 Jan., 1998

1998

MEDIUM: print

ISSN: 0954-7894

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

1998

...ABSTRACT: increase in albumin levels and a trend in total protein levels. Conclusions. We conclude that **nonallergic rhinitis** is not characterized by increased responsiveness of capsaicin-sensitive nerve fibres; while allergic rhinitis is...

DESCRIPTORS:

...DISEASES: immune system disease, **respiratory** system disease...

... **respiratory** system disease

5/3,K/22

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0011306392 BIOSIS NO.: 199800100639

Mucoglycoprotein hypersecretion in allergic rhinitis and cystic fibrosis

AUTHOR: Yuta Atsushi; Ali Mushtaq; Sabol Marybeth; Gaumond Ethan; Baraniuk James N (Reprint)

AUTHOR ADDRESS: Div. Rheumatol. Immunol. Allergy, GL-008, Gorman Building,
Georgetown Univ. Med. Cent., 3800 Reservoir Rd. NW, Washington, DC
20007-2197, USA**USA

JOURNAL: American Journal of Physiology 273 (6 PART 1): pL1203-L1207 Dec.,
1997 1997

MEDIUM: print

ISSN: 0002-9513

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

1997

...ABSTRACT: information about specific changes in submucosal gland
exocytosis in diseases such as allergic rhinitis (AR), **nonallergic
rhinitis** (NAR), and cystic fibrosis (CF). Nasal lavage fluids were
collected from normal, AR, NAR, and...

DESCRIPTORS:

MAJOR CONCEPTS: **Respiratory** System...

... **Respiration**

...DISEASES: **respiratory** system disease...

...digestive system disease, genetic disease, metabolic disease,
respiratory system disease...

... **nonallergic rhinitis** --...

... **respiratory** system disease

5/3,K/23

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0011306373 BIOSIS NO.: 199800100620

**Bronchial responsiveness and airway inflammation in patients with
nonallergic rhinitis with eosinophilia syndrome**

AUTHOR: Leone Clementina; Teodoro Concetta; Pelucchi Andrea; Mastropasqua
Berardino; Cavigioli Giampaolo; Marazzini Luigi; Foresi Antonio (Reprint)

AUTHOR ADDRESS: Servizio di Fisiopatol. Respir., Viale Matteotti 83, 20099
Sesto San Giovanni, Italy**Italy

JOURNAL: Journal of Allergy and Clinical Immunology 100 (6 PART 1): p
775-780 Dec., 1997 1997

MEDIUM: print

ISSN: 0091-6749

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Bronchial responsiveness and airway inflammation in patients with

nonallergic rhinitis with eosinophilia syndrome
1997

ABSTRACT: Background: **Nonallergic rhinitis** with eosinophilia syndrome (NARES) is characterized by persistent nasal symptoms without allergy and by a...

...excluded by skin prick tests and RASTs. None of the patients had a history of **respiratory** symptoms. We preliminarily performed nasal lavage in all patients, and the diagnosis of NARES was...

...0.001). Conclusion: We showed that 46% of patients with NARES but without histories of **respiratory** symptoms had a measurable bronchial responsiveness. The presence of bronchial responsiveness was associated with an...

DESCRIPTORS:

...DISEASES: **respiratory** system disease...

... **nonallergic rhinitis** --...

... **respiratory** system disease

5/3,K/24

DIALOG(R) File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0011066129 BIOSIS NO.: 199799700189

Air pollution in relation to allergic and nonallergic rhinitis

AUTHOR: Samir Magdy (Reprint); Magdy Sabry; El Fetoh Aisha A

AUTHOR ADDRESS: 12Ibn El Wardy St., Hegaz Square, Heliopolis, Cairo, Egypt
**Egypt

JOURNAL: Archives of Otolaryngology Head and Neck Surgery 123 (7): p
746-748 1997 1997

ISSN: 0886-4470

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Air pollution in relation to allergic and nonallergic rhinitis
1997

ABSTRACT: Objective: To investigate the relationship between allergic and **nonallergic rhinitis** and the exposure to air pollution. Design: Blood cadmium levels were measured in 30 patients with allergic rhinitis, 30 patients with **nonallergic rhinitis**, and 16 normal control subjects using atomic absorption spectrophotometry. The cadmium level was used as ...

...Results: Blood cadmium levels were significantly high in the allergic rhinitis group compared with the **nonallergic rhinitis** and control groups (P lt .001). The mean blood cadmium level in the **nonallergic rhinitis** group was higher than that in the controls, yet the difference was statistically insignificant. Also...

...between air pollution and this condition. The exact mechanism, however, remains to be determined. In **nonallergic rhinitis**, it seems that the contribution of air pollution as a predisposing factor is small compared ...

DESCRIPTORS:

...MAJOR CONCEPTS: **Respiratory** System...

... **Respiration ;**
MISCELLANEOUS TERMS: ... **NONALLERGIC RHINITIS ; ...**

... **RESPIRATORY SYSTEM...**

... **RESPIRATORY SYSTEM DISEASE**

5/3,K/25

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0011004356 BIOSIS NO.: 199799638416

Rhinopharyngoscopy, computed tomography and magnetic resonance imaging

AUTHOR: Bonifazi F (Reprint); Bilo M B; Antonicelli L; Bonetti M G

AUTHOR ADDRESS: Allergy Respiratory Unit, Regional Hosp., Largo Cappelli 1,
60100 Ancona, Italy**Italy

JOURNAL: Allergy (Copenhagen) 52 (SUPPL. 33): p28-31 1997 **1997**

ISSN: 0105-4538

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

1997

...ABSTRACT: one of the most useful diagnostic tools in the complex
differential diagnosis between allergic and **nonallergic rhinitis** .
Furthermore, chronic allergic rhinitis, with secondary impairment of
mucociliary clearance and the plethora of frequent...

DESCRIPTORS:

MISCELLANEOUS TERMS: ... **RESPIRATORY SYSTEM...**

... **RESPIRATORY SYSTEM DISEASE**

5/3,K/26

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0010987660 BIOSIS NO.: 199799621720

Nasal polyposis, sinusitis, and nonallergic rhinitis

BOOK TITLE: Allergic diseases: Diagnosis and management

AUTHOR: Bernstein David I

BOOK AUTHOR/EDITOR: Patterson R (Editor)

AUTHOR ADDRESS: Div. Immunol., ML563, Univ. Cincinnati Coll. Med.,
Cincinnati, OH 45267-0563, USA**USA

p425-437 **1997**

BOOK PUBLISHER: Lippincott-Raven Publishers {a}, 227 East Washington
Square, Philadelphia, Pennsylvania 19106, USA

ISBN: 0-397-51609-6

DOCUMENT TYPE: Book Chapter

RECORD TYPE: Citation

LANGUAGE: English

Nasal polyposis, sinusitis, and nonallergic rhinitis

1997

DESCRIPTORS:

MISCELLANEOUS TERMS: ... **NONALLERGIC RHINITIS ; ...**

... **RESPIRATORY** **SYSTEM DISEASE**

5/3,K/27

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0010915730 BIOSIS NO.: 199799549790

**Nasal biopsy is superior to nasal smear for finding eosinophils in
nonallergic rhinitis**

AUTHOR: Ingels K (Reprint); Durdurez J-P; Cuvelier C; Van Cauwenberge P

AUTHOR ADDRESS: Academic Hosp. Nijmegen St. Radboud, Dep.

Otorhinolaryngol., Geert Grooteplein Zuid 18, 6525 GA Nijmegen,
Netherlands**Netherlands

JOURNAL: Allergy (Copenhagen) 52 (3): p338-341 1997 **1997**

ISSN: 0105-4538

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

**Nasal biopsy is superior to nasal smear for finding eosinophils in
nonallergic rhinitis**

1997

ABSTRACT: The presence of eosinophils was compared in nasal biopsy and
smear. Thirty-two **nonallergic rhinitis** patients, of whom six had
nasal polyps, were included in the study. The specimens were...

...at least four eosinophils in four fields as hypereosinophilic, our group
of patients contained 25% **nonallergic rhinitis** with eosinophilia
syndrome (NARES) patients.

DESCRIPTORS:

...MAJOR CONCEPTS: **Respiratory** **System...**

... **Respiration** ;

MISCELLANEOUS TERMS: ... **NONALLERGIC** **RHINITIS** ; ...

... **RESPIRATORY** **SYSTEM DISEASE**

5/3,K/28

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0010810453 BIOSIS NO.: 199799444513

**Patient-rated overall treatment satisfaction and effectiveness with three
dosing regimens of intranasal fluticasone propionate (FP) in perennial
nonallergic rhinitis (PNAR)**

AUTHOR: Pepsin P J (Reprint); Howlandi W C II; Finn A F Jr; Cox F M; Bowers
B W; Montgomery E; Westlung R

AUTHOR ADDRESS: HealthQuest Therapy Res. Inst. Inc., Austin, TX, USA**USA

JOURNAL: Journal of Allergy and Clinical Immunology 99 (1 PART 2): pS442
1997 **1997**

CONFERENCE/MEETING: Joint Meeting of the American Academy of Allergy,
Asthma and Immunology, the American Association of Immunologists and the
Clinical Immunology Society San Francisco, California, USA February
21-26, 1997; 19970221

ISSN: 0091-6749

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

...treatment satisfaction and effectiveness with three dosing regimens of intranasal fluticasone propionate (FP) in perennial nonallergic rhinitis (PNAR)

1997

DESCRIPTORS:

MISCELLANEOUS TERMS: ...PERENNIAL NONALLERGIC RHINITIS ; ...

... RESPIRATORY SYSTEM DISEASE

5/3,K/29

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0010810444 BIOSIS NO.: 199799444504

Efficacy of three different dosing regimens of fluticasone propionate (FP) aqueous nasal spray in the treatment of perennial nonallergic rhinitis (PNAR)

AUTHOR: Finn A F Jr (Reprint); Howlandi W C II; Bronsky E A; Lumry W R; Pepsin P J; Rogenes P R; Westlund R; Cook C K

AUTHOR ADDRESS: Charleston, SC, USA**USA

JOURNAL: Journal of Allergy and Clinical Immunology 99 (1 PART 2): pS440
1997 1997

CONFERENCE/MEETING: Joint Meeting of the American Academy of Allergy, Asthma and Immunology, the American Association of Immunologists and the Clinical Immunology Society San Francisco, California, USA February 21-26, 1997; 19970221

ISSN: 0091-6749

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

...different dosing regimens of fluticasone propionate (FP) aqueous nasal spray in the treatment of perennial nonallergic rhinitis (PNAR)

1997

DESCRIPTORS:

MISCELLANEOUS TERMS: ...PERENNIAL NONALLERGIC RHINITIS ; ...

... RESPIRATORY SYSTEM DISEASE

5/3,K/30

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0010810367 BIOSIS NO.: 199799444427

Elastase in nasal lavage of cystic fibrosis and chronic fatigue syndrome (CFS) subjects with nonallergic rhinitis (NAR)

AUTHOR: Yuta A (Reprint); Fujita K (Reprint); Shimizu T (Reprint); Ali M; Clauw D; Baraniuk J N

AUTHOR ADDRESS: Mie Univ., Mie, Japan**Japan

JOURNAL: Journal of Allergy and Clinical Immunology 99 (1 PART 2): pS420
1997 1997

CONFERENCE/MEETING: Joint Meeting of the American Academy of Allergy, Asthma and Immunology, the American Association of Immunologists and the Clinical Immunology Society San Francisco, California, USA February 21-26, 1997; 19970221

ISSN: 0091-6749

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation
LANGUAGE: English

Elastase in nasal lavage of cystic fibrosis and chronic fatigue syndrome (CFS) subjects with nonallergic rhinitis (NAR) 1997

DESCRIPTORS:

MISCELLANEOUS TERMS: ... NONALLERGIC RHINITIS ; ...

... RESPIRATORY SYSTEM DISEASE

5/3,K/31

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0010810366 BIOSIS NO.: 199799444426

Nonallergic rhinitis (NAR) of chronic fatigue syndrome (CFS)

AUTHOR: Ali M; Gaumond E; Yuta A; Clauw D; Baraniuk J N

AUTHOR ADDRESS: Georgetown Univ., Washington, DC, USA**USA

JOURNAL: Journal of Allergy and Clinical Immunology 99 (1 PART 2): pS420
1997 1997

CONFERENCE/MEETING: Joint Meeting of the American Academy of Allergy, Asthma and Immunology, the American Association of Immunologists and the Clinical Immunology Society San Francisco, California, USA February 21-26, 1997; 19970221

ISSN: 0091-6749

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

Nonallergic rhinitis (NAR) of chronic fatigue syndrome (CFS)
1997

DESCRIPTORS:

MISCELLANEOUS TERMS: ... NONALLERGIC RHINITIS ; ...

... RESPIRATORY SYSTEM DISEASE

5/3,K/32

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0010745916 BIOSIS NO.: 199799379976

Existence of c-kit receptor-positive, tryptase-negative, IgE-negative cells in human allergic nasal mucosa: A candidate for mast cell progenitor

AUTHOR: Kawabori Shinichi (Reprint); Kanai Naoki; Tosho Takuro; Adachi Toshihide

AUTHOR ADDRESS: Dep. Otolaryngol., Asahikawa Medical Sch., Nishikagura 4-5-3-11, Asahikawa 078, Japan**Japan

JOURNAL: International Archives of Allergy and Immunology 112 (1): p36-43
1997 1997

ISSN: 1018-2438

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

1997

...ABSTRACT: in the nasal mucosae of 11 patients with nasal allergy and of

5 patients with **nonallergic rhinitis** . From one to four of these cells in the nasal epithelium and subepithelial layer of...

DESCRIPTORS:

MISCELLANEOUS TERMS: ... **RESPIRATORY SYSTEM**

5/3,K/33

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0010739112 BIOSIS NO.: 199799373172

Differences in nonspecific bronchial responsiveness between patients with asthma and patients with rhinitis are not explained by type and degree of inhalant allergy

AUTHOR: Witteman Agnes M; Sjamsoedin Deman H S; Jansen Henk M; Van Der Zee Jaring S (Reprint)

AUTHOR ADDRESS: Academic Medical Cent., Univ. Amsterdam, Dep. Pulmonol., F4-239, PO Box 22700, NL-1100 DE Amsterdam, Netherlands**Netherlands

JOURNAL: International Archives of Allergy and Immunology 112 (1): p65-72
1997 1997

ISSN: 1018-2438

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

1997

...ABSTRACT: as confounding variables. In addition, a matched pair analysis was performed. Twenty-five patients with **nonallergic rhinitis** served as controls to evaluate the influence of an IgE-independent inflammatory reaction in the upper **respiratory** tract on the level of bronchial responsiveness. Furthermore, we investigated the level of nonspecific responsiveness...

...patients, the difference in level of bronchial responsiveness remained (p lt 0.001). Patients with **nonallergic rhinitis** had higher levels of nonspecific bronchial responsiveness than healthy controls and did not differ from...

DESCRIPTORS:

MISCELLANEOUS TERMS: ... **RESPIRATORY SYSTEM DISEASE**

5/3,K/34

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0010663876 BIOSIS NO.: 199799297936

A study of clinical and allergic aspects of rhinitis patients in Riyadh

AUTHOR: Zakzouk Siraj Mustafa; Gad-El-Rab Mohamed Osman

AUTHOR ADDRESS: Dep. ENT, King Abdulaziz Univ. Hosp., P.O Box 245, Riyadh 11411, Saudi Arabia**Saudi Arabia

JOURNAL: Annals of Saudi Medicine 16 (5): p550-553 1996 1996

ISSN: 0256-4947

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

1996

...ABSTRACT: investigated. Fifty-three (66.25%) were identified as allergic

and 27 (33.5%) as having **nonallergic rhinitis** . Medical history and clinical examination alone seemed to be inadequate in establishing a diagnosis, since...

DESCRIPTORS:

MISCELLANEOUS TERMS: ... **RESPIRATORY SYSTEM DISEASE**

5/3,K/35

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0010663143 BIOSIS NO.: 199799297203

Rhinitis in Singapore

AUTHOR: Yeak S (Reprint); John A B; Chee N; Chng H H

AUTHOR ADDRESS: Dep. Otolaryngol., Tan Tock Seng Hosp., Moulmein Road, 308433, Singapore**Singapore

JOURNAL: Allergy (Copenhagen) 51 (10): p757-758 1996 **1996**

ISSN: 0105-4538

DOCUMENT TYPE: Article

RECORD TYPE: Citation

LANGUAGE: English

1996

DESCRIPTORS:

MISCELLANEOUS TERMS: ... **NONALLERGIC RHINITIS ; ...**

... **RESPIRATORY SYSTEM...**

... **RESPIRATORY SYSTEM DISEASE**

5/3,K/36

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0010060224 BIOSIS NO.: 199598528057

Allergy of the upper respiratory tract

BOOK TITLE: Manual of allergy and immunology, Third edition

AUTHOR: Lierl Michelle B

BOOK AUTHOR/EDITOR: Lawlor G J (Editor); Fischer T J (Editor); Adelman D C (Editor)

AUTHOR ADDRESS: Univ. Cincinnati, Coll. Med., Div. Allergy/Immunol., Cincinnati, OH, USA**USA

p94-111 **1995**

BOOK PUBLISHER: Little, Brown and Co., 34 Beacon Street, Boston, Massachusetts 02108, USA

Little, Brown and Co., London, England, UK

ISBN: 0-316-51681-3

DOCUMENT TYPE: Book; Book Chapter

RECORD TYPE: Citation

LANGUAGE: English

Allergy of the upper respiratory tract

1995

DESCRIPTORS:

...MAJOR CONCEPTS: **Respiratory System...**

... **Respiration ;**

MISCELLANEOUS TERMS: ... **NONALLERGIC RHINITIS WITH EOSINOPHILIA SYNDROME**

5/3,K/37

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0009545348 BIOSIS NO.: 199598013181

**The usefulness of the nasal smear in understanding the relationship between
nonallergic rhinitis with eosinophilia and recurrent purulent
rhinitis**

AUTHOR: Mansmann Paris T

AUTHOR ADDRESS: West Virginia Univ., Box 9167 Health Sci. Center,
Morgantown, WV 26506-9167, USA**USA

JOURNAL: Pediatric Asthma Allergy and Immunology 8 (2): p117-119 1994
1994

ISSN: 0883-1874

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

**The usefulness of the nasal smear in understanding the relationship between
nonallergic rhinitis with eosinophilia and recurrent purulent
rhinitis**
1994

ABSTRACT: Review of the literature classifies nonallergic rhinitis with
eosinophilia as a separate entity from purulent rhinitis, chronic
sinusitis, and chronic hyperplastic sinusitis...

DESCRIPTORS:

...MAJOR CONCEPTS: Respiratory System...

... Respiration

5/3,K/38

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0009434545 BIOSIS NO.: 199497455830

Treatment modalities and drugs used in vasomotor rhinitis

AUTHOR: Dainyak L B

AUTHOR ADDRESS: Sci. Cent. Audiol. Hear. Aids, Minist. Health Russ.,
Moscow, Russia**Russia

JOURNAL: Vestnik Otorinolaringologii 0 (4): p36-41 1993 1993

ISSN: 0042-4668

DOCUMENT TYPE: Article

RECORD TYPE: Citation

LANGUAGE: Russian

1993

DESCRIPTORS:

...MAJOR CONCEPTS: Respiratory System...

... Respiration ;

MISCELLANEOUS TERMS: ... NONALLERGIC RHINITIS ;

5/3,K/39

DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0009383011 BIOSIS NO.: 199497404296

Synthesis of interleukin-1-alpha, interleukin-6, and interleukin-8 by cultured human nasal epithelial cells

AUTHOR: Kenney John S; Baker Coralie; Welch Mary R; Altman Leonard C
(Reprint)

AUTHOR ADDRESS: Div. Allergy Infect. Dis., Dep. Med., SJ-10, Univ. Wash.,
Seattle, WA 98195, USA**USA

JOURNAL: Journal of Allergy and Clinical Immunology 93 (6): p1060-1067
1994 1994

ISSN: 0091-6749

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

1994

ABSTRACT: Nasal epithelium forms the initial barrier between the environment and the **respiratory** system and may be a potential source of proinflammatory interleukins, which contribute to the pathophysiology of allergic and **nonallergic rhinitis**. To explore this possibility, epithelium and cultured human nasal epithelial cells from nasal turbinates of...

...a major source of IL-1-alpha, IL-6, and IL-8 in allergic and **nonallergic rhinitis**. Production of those proinflammatory cytokines by epithelial cells of the nasal and sinus mucosa may...

DESCRIPTORS:

...MAJOR CONCEPTS: **Respiratory** System...

... **Respiration**

5/3,K/40

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0009059040 BIOSIS NO.: 199497080325

Pathophysiology and pharmacotherapy of common upper respiratory diseases

AUTHOR: Fireman Philip

AUTHOR ADDRESS: Children's Hospital, 3705 Fifth Ave., Pittsburgh, PA 15213,
USA**USA

JOURNAL: Pharmacotherapy 13 (6 PART 2): p101S-109S 1993 1993

ISSN: 0277-0008

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Pathophysiology and pharmacotherapy of common upper respiratory diseases
1993

ABSTRACT: The response of the upper **respiratory** tract to many environmental factors can be used both to analyze the body's inflammatory ...

...and its reactions often represent a major portion of the problem. The most common upper **respiratory** illnesses are upper **respiratory** infections (URIs), primarily viral, followed by secondary bacterial infections. Approximately 20% of the total population...

...is no direct allergy to hay, and there is no fever. The differential

diagnosis includes **nonallergic rhinitis** with eosinophils, which mimics the pathophysiology of allergic rhinitis but yields negative results on skin...

...adrenergic agonists are the optimum choices for congestion associated with viral URIs, and allergic or **nonallergic rhinitis**. Of major importance are accurate diagnosis, selection of appropriate therapy, and patient compliance.

DESCRIPTORS:

...MAJOR CONCEPTS: **Respiratory** System...

... **Respiration** ;

5/3,K/41

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0009003161 BIOSIS NO.: 199497024446

In vivo detection of a novel macrophage-derived protein involved in the regulation of nasal mucus-like glycoconjugate secretion

AUTHOR: Sperber Kirk (Reprint); Sylvester Clewert; Gollub Edith; Goswami Satindra; Kalb Thomas H; Druce Howard; Rutledge Joyce; Marom Zvi

AUTHOR ADDRESS: Div. Clinical Immunol., Box 1089, 1 Gustave Levy Pl., New York, NY 10029, USA**USA

JOURNAL: Journal of Allergy and Clinical Immunology 92 (4): p581-588 1993
1993

ISSN: 0091-6749

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

1993

...ABSTRACT: D-10) on frozen sections (n = 5) of nasal turbinates from patients with allergic and **nonallergic rhinitis** who were undergoing rhinoplasty and measured MMS-68 levels in nasal lavages from patients who

...

DESCRIPTORS:

...MAJOR CONCEPTS: **Respiratory** System...

... **Respiration**

MISCELLANEOUS TERMS: ALLERGIC VS. **NONALLERGIC** RHINITIS PATIENT...

5/3,K/42

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0007708908 BIOSIS NO.: 199191091799

HISTAMINE CHALLENGING TEST ON THE NASAL MUCOSA OF THE PATIENTS WITH ALLERGIC RHINITIS

AUTHOR: YANG P (Reprint); TAO Z

AUTHOR ADDRESS: DEP OTOLARYNGOL, FIRST AFFILIATED HOSP, HUNAN MED UNIV** CHINA

JOURNAL: Hunan Yike Daxue Xuebao 15 (4): p369-371 **1990**

ISSN: 1000-5625

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: CHINESE

1990

ABSTRACT: Ninety-six patients with perennial allergic rhinitis, 20 patients with either vasomotor or eosinophilic **nonallergic rhinitis**, and 33 healthy subjects were all challenged with topical application 10-3M histamine on the...

DESCRIPTORS:

...MAJOR CONCEPTS: **Respiratory System**...

... **Respiration** ;

5/3,K/43

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0007259093 BIOSIS NO.: 199090043572

EFFICACY AND SAFETY OF INTRANASAL BUDESONIDE IN THE TREATMENT OF PERENNIAL RHINITIS IN ADULTS AND CHILDREN

AUTHOR: DAY J H (Reprint); ANDERSSON C B; BRISCOE M P

AUTHOR ADDRESS: DIV ALLERGY IMMUNOLOGY, KINGSTON GENERAL HOSP, KINGSTON, ONTARIO, CANADA K7L 2V7**CANADA

JOURNAL: Annals of Allergy 64 (5): p445-450 1990

ISSN: 0003-4738

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

1990

...ABSTRACT: study of 51 children (6 to 18 years) and 48 adults with perennial (allergic or **nonallergic**) **rhinitis**. The trial commenced with a 2-week baseline period without treatment for perennial rhinitis. This...

DESCRIPTORS:

...MAJOR CONCEPTS: **Respiratory System**...

... **Respiration**

5/3,K/44

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0005361332 BIOSIS NO.: 198732090223

SACCHARIN-BISMUTH SUBGALLATE S-BSG TEST FOR NASAL MUCOCILIARY CLEARANCE NMC AN IMPROVED METHOD

AUTHOR: HUBBLE M A (Reprint); JALOWAYSKI A A; MELTZER E O; KEMP J P

AUTHOR ADDRESS: SAN DIEGO, CALIF, USA**USA

JOURNAL: Journal of Allergy and Clinical Immunology 79 (1): p254 1987

CONFERENCE/MEETING: FORTY-THIRD ANNUAL MEETING OF THE AMERICAN ACADEMY OF ALLERGY AND IMMUNOLOGY, WASHINGTON, D.C., USA, FEB. 19-25, 1987. J ALLERGY CLIN IMMUNOL.

ISSN: 0091-6749

DOCUMENT TYPE: Meeting

RECORD TYPE: Citation

LANGUAGE: ENGLISH

1987

DESCRIPTORS: ABSTRACT HUMAN ALLERGIC RHINITIS NONALLERGIC RHINITIS

DESCRIPTORS:

...MAJOR CONCEPTS: Respiratory System...

... Respiration

5/3,K/45

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0004800235 BIOSIS NO.: 198580109130

**AN IMMUNOHISTOCHEMICAL STUDY OF PLASMA CELLS IN HUMAN ALLERGIC AND
NON-ALLERGIC RHINITIS**

AUTHOR: AE H J (Reprint); YOEM B W; LEE D

AUTHOR ADDRESS: DEP PATHOL, COLL MED, KOREA UNIV**SOUTH KOREA

JOURNAL: Korea University Medical Journal 22 (1): p205-214 1985

ISSN: 0378-648X

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: KOREAN

1985

...ABSTRACT: of allergic rhinitis, was invariably noted in the clinical entity such as nasal polyposis, perennial nonallergic rhinitis and aspirin intolerance. An experimental study was performed using rabbit antihuman IgG, IgM, and IgA on the tissue sections of nasal mucosa to find differences between allergic and nonallergic rhinitis. In nonallergic rhinitis, all the cases examined showed plasma cells which react to antihuman IgG and IgA especially...

...the cases of allergic rhinitis. It seems to be possible to differentiate allergic rhinitis from nonallergic rhinitis by the scarcity of plasma cells which react antihuman IgG antibody and increase in numbers...

DESCRIPTORS:

...MAJOR CONCEPTS: Respiratory System...

... Respiration

5/3,K/46

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 BIOSIS. All rts. reserv.

0002961740 BIOSIS NO.: 198069075727

**ALLERGIC AND NONALLERGIC RHINITIS THEIR CHARACTERIZATION WITH ATTENTION
TO THE MEANING OF NASAL EOSINOPHILIA**

AUTHOR: MULLARKEY M F (Reprint); HILL J S; WEBB D R

AUTHOR ADDRESS: SECT IMMUNOL ALLERGY RHEUMATIC DIS, DEP MED, MASON CLIN,
1100 NINTH AVE, SEATTLE, WASH 98101, USA**USA

JOURNAL: Journal of Allergy and Clinical Immunology 65 (2): p122-126 1980

ISSN: 0091-6749

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

**ALLERGIC AND NONALLERGIC RHINITIS THEIR CHARACTERIZATION WITH ATTENTION
TO THE MEANING OF NASAL EOSINOPHILIA**

1980

ABSTRACT: The differences between allergic and **nonallergic rhinitis** were examined. Patients (142) were evaluated. Forty-eight patients were diagnosed as having allergic rhinitis...

...no evidence for immunologic nasal disease, incriminated physical agents as precipitants, and demonstrated no associated **respiratory** pathology. These patients were classified as having vasomotor rhinitis (VMR). Twenty-one patients had symptoms...

...of patients with VMR, but they demonstrated nasal eosinophilia and were classified as having eosinophilic **nonallergic rhinitis** (ENR). These patients had a high prevalence of nasal polyps and were significantly more responsive...

...value in the evaluation of AR but provides significant information regarding therapy and prognosis in **nonallergic rhinitis**.

? logoff

```
24may06 08:18:01 User291213 Session D23.2
$10.31      1.747 DialUnits File5
      $7.36  46 Type(s) in Format 95 (KWIC)
      $7.36  46 Types
$17.67 Estimated cost File5
$1.06  TELNET
$18.73 Estimated cost this search
$19.15 Estimated total session cost   1.861 DialUnits
```

Logoff: level 05.11.05 D 08:18:01

You are now logged off